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Does liberalisation of cannabis policy influence levels of use in adolescents and young adults? A systematic review

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Keywords : cannabis, marijuana, decriminalisation, legalisation, epidemiology, adolescents, young adults

Abstract

Objective: To examine the effect of the introduction of policies liberalising cannabis use and possession (decriminalisation, legalisation) on adolescents' and young adults' use.

Design: Systematic review and meta-analysis.

Methods: Articles were searched for in Pubmed, PsycINFO, Embase and Web of Science up to March 2018 following PRISMA guidelines. Search terms (law* OR decriminalisation OR legalisation) AND (cannabis OR pot OR weed OR marijuana OR grass) AND (young OR youth OR adolescen* OR teen* OR school* OR student) were looked for in MeSH terms and in the text. Two independent readers reviewed the eligibility of titles and abstracts, read eligible articles, and four authors assessed the risk of bias (Quality Assessment Tool for Observational Cohort and Cross-Sectional Studies). Extracted data were meta-analysed. The protocol was registered with PROSPERO (CRD42018083950).

Outcome measures: Standardised Mean Differences in cannabis use (30 days, 12 months, lifetime, age of initiation); sensitivity analyses focused on recent use (30 days).

Results: Altogether, 3438 records were identified via search terms and 4 via citation lists; 2312 were retained after removal of duplicates, 99 were assessed for eligibility and 41 original research reports were included in our systematic review. Among them, 13 examined cannabis decriminalisation, 20 legalisation for medical purposes and 8 legalisation for recreational purposes. Findings regarding the consequences of cannabis decriminalisation or legalisation for medical purposes were too heterogeneous to be meta-analysed.

Nevertheless, studies characterised by a very low/low risk of bias showed no evidence of changes in cannabis use following policy modifications. Our systematic review and meta-analysis suggest a small increase in cannabis use among adolescents and young adults following legalisation of cannabis for recreational purposes.

Conclusions: Cannabis policy liberalisation does not appear to result in significant changes in youths' use, with the possible exception of legalisation for recreational purposes which requires monitoring over time.

Strengths and limitations of this study

- Specific provisions of laws and policies regulating cannabis vary across settings, therefore policy changes examined could be heterogeneous.
- The duration of follow-up varied across studies, partly because changes in cannabis policy occurred in different periods and places.
- Among studies examining the consequences of the legalisation of cannabis for recreational purposes, only one was characterised by a very low risk of bias and 5 by a low risk of bias, therefore the findings will need to be confirmed in future research.

Introduction

Cannabis is one of the most frequently used psychoactive substances in North America, Europe, Oceania, and North Africa (12-month prevalence of 3.8% in the world)[1]. Since the 1961 Single Convention on Narcotic Drugs, cannabis is illegal in most countries. However, in the past 20 years a majority of US states (thirty one including the District of Columbia) and several countries (e.g. Spain, Uruguay, Portugal) have liberalised their cannabis legislation by decriminalising or legalising use for medical or recreational purposes[2]. Decriminalisation is the reduction of penalties for cannabis use, while maintaining penalties for cannabis supply. Legalisation is the permission to use and supply oneself (via home growing or controlled sale). Legalisation for medical use is permission to use and sometimes supply with the involvement of a medical professional (e.g. with a doctor's prescription or recommendation)[3].

In many settings - especially where cannabis is widely used – public support for legalisation is widespread[4 5]. For cannabis users, decriminalised or regulated access to the substance decreases the legal and criminal risks incurred. Potential collective benefits of cannabis policy liberalisation include: a) reduced law enforcement costs, b) improvements in the quality of the substance used, c) in case of commercial legalisation, additional tax revenue[6].

Still, cannabis is a source of addiction and can have deleterious health consequences in the short and long-terms, including impairments in memory and concentration[7], risk of injury, or respiratory problems[8]. Moreover, liberalised access to cannabis could also influence the levels of use of other psychoactive substances (e.g. tobacco, alcohol)[9 10]. At the same time, there is also evidence that in the United States, the recent increase in opioid use

is less marked in states which recently implemented policies liberalising cannabis regulations[11].

In adults, the liberalisation of cannabis policy has been followed by increases in levels of heavy cannabis use[12]. This may be driven by reductions in the perceived risks[13], price decreases, as well as increases in cannabis availability[12 14]. However, in adolescents, who may be especially vulnerable to the negative consequences of cannabis[7], the impact of policy liberalisation is unclear[12]. As additional US states and European countries are considering liberalising cannabis legislation, there is need to evaluate the potential public health consequences of such policy change.

To gain better understanding of the influence of changes in cannabis policy on patterns of use among adolescents and young adults, we systematically reviewed and meta-analysed data published before 2018 on this topic.

Methods

Search strategy

Following PRISMA guidelines[15], we conducted a systematic review of studies testing quantitative differences in cannabis use among adolescents and young adults before and after policy change, published prior to March 1, 2018.

Specifically, the following search terms were introduced in Pubmed, Web of Science, EMBASE, PsycINFO: (law* OR decriminalisation OR legalisation) AND (cannabis OR pot OR weed OR marijuana OR grass) AND (young OR youth OR adolescen* OR teen* OR school* OR student). Searches were specified for both MeSH terms and text words and were modified to meet the requirements of each database. Only articles in English were identified. All titles and abstracts were independently screened by two of the authors to determine potential eligibility. Full texts of all potentially eligible studies were read by two of the authors (FH,

MAdS) and discussed with all other authors in case of disagreement. The protocol was registered in PROSPERO (CRD42018083950) and followed the PRISMA framework[15].

Inclusion criteria

To be included, studies had to quantitatively assess cannabis use before and after policy change (defined as decriminalisation, or legalisation of cannabis use for medical or recreational purposes) among individuals younger than 25 years. This age limit was selected as it is a meaningful cut-off for the potentially negative biological and social effects of cannabis[7] as well as a frequently-used upper bound to define young people. We excluded articles: a) exclusively based on participants older than 25 years; b) only reporting changes in perceptions of cannabis use; c) not including at least two measures of cannabis use; d) not including quantitative data; e) reviews, letters, opinions and policy papers.

Risk of bias

Risk of bias was assessed using the Quality Assessment Tool for Observational Cohort and Cross-Sectional Studies developed by the National Institute of Health (NIH) (https://www.nhlbi.nih.gov/health-pro/guidelines/in-develop/cardiovascular-risk-reduction/tools/cohort). Two independent raters evaluated each study on up to 11 items including characteristics of the study population, exposure and outcome measurement, time frame adequacy, loss to follow-up (cohort studies; <20% being considered as associated with low bias), adjustment for confounders. This yielded a rating of very low, low, possible or probable risk of bias for each study. Studies defined as presenting a very low risk of bias had no identified flaws. Studies characterised by a low risk of bias provided insufficient information regarding the study time frame or loss to follow-up (where applicable). Studies considered to present a possible risk of bias were characterised by any of the following: a) insufficient information about the study population recruitment or follow-up (where

applicable), b) insufficient definition of exposure or outcome, c) a study period of < 1 year between exposure and outcome, or d) insufficient adjustment for potentially confounding individual or contextual factors. Studies considered to present a probable risk of bias were characterised by two or more of the risks identified above. Differences in ratings between coders were discussed in joint meetings.

Data extraction

A coding sheet was developed to identify: study authors, setting, type of policy change/ study period, inclusion criteria/numbers of subjects (ns), study design, cannabis use measure, statistical methods used/covariates controlled for, key findings and estimated level of bias.

Meta-analysis

To meta-analyse the effects of the liberalisation of cannabis policy on levels of use, we calculated Standardised Mean Differences (SMD) and associated 95% confidence intervals for each finding using the Practical Meta-Analysis Effect Size Calculator[16]. Effects sizes from different studies were combined into a weighted mean effect size. Each effect size was weighted by the inverse of its variance and then averaged[17]. Standard meta-analytical procedures suppose the independence of effects[18]. However, several primary studies provided multiple correlated effect size estimates for the same underlying outcome (e.g. 30-day use, 12-month use etc.). To avoid the loss of information resulting from the selection of only one effect size per study, we used the Robust Variance Estimation (RVE) method[19], which makes it possible to handle statistically dependent effect sizes. A fixed effect meta-analysis was undertaken in the absence of heterogeneity, otherwise a random effects model was used [20]. To test for homogeneity, we computed the Q statistic to determine whether each set of effect sizes shared a common population effect size[17]. To interpret between-

study heterogeneity, we used the I^2 statistic; an $I^2 > 50\%$ was considered to indicate important heterogeneity[21].

To study whether cannabis use in adolescents and young adults varied as a function of 1) cannabis decriminalisation, 2) legalisation of cannabis use for medical purposes or 3) legalisation of cannabis use for recreational purposes, we conducted three main meta-analyses.

For each type of cannabis policy change, we also performed a priori hypothesised subgroup analyses, according to study design (cohort vs. cross-sectional), study year (< 2000 vs. ≥ 2000), participants' age (< vs. ≥ 18 years) and the measure of cannabis use (30-day use vs. 12-month use). Studies included in this review did not present stratified results based on whether participants were < vs. ≥ 21 years (the legal age for cannabis use in US states which legalised the substance), making it impossible for us to conduct sensitivity analyses using this age cut-off.

Finally, because the results of a meta-analysis can be biased by studies with non-significant results being less likely to be published, we examined publication bias graphically, using a funnel plot. All analyses were performed using STATA 14.0 and the *robumeta* macro [22].

Results

As shown in the study flowchart (**Figure 1**), our initial search identified 3438 titles of potentially relevant articles, among which 3293 were in English. After the removal of 981 duplicates, 2312 abstracts were screened independently by two of the authors. This lead to the removal of 2213 articles that did not focus on changes in cannabis use, as well as letters, reviews, commentaries, editorials, or errata. In total, 99 full-text articles were accessed and evaluated for eligibility. Of those, 58 articles were excluded because they did not provide

data on patterns of cannabis use before and after policy change. This yielded 41 original research reports to be analysed.

The 41 studies analysed were all published in English: 33 were conducted in the United States[23-55], 3 in Australia[56-58], 2 in the United Kingdom[59 60], 1 in the Netherlands[61], 1 in the Czech Republic[62], and 1 internationally[63]. Thirteen studies evaluated the consequences of cannabis decriminalisation[23-26 35 56-63], 20 the consequences of legalisation of use for medical purposes[27-34 36-43 47 51-53], and 8 the consequences of legalisation of use and possession for recreational purposes[44-46 48-50 54 55]. All studies examining the effects of cannabis legalisation (for medical or recreational purposes) were based in the United States.

The reports included were somewhat heterogeneous in terms of the populations studied: 21 focused on adolescents (12-17 years)[23 26 29 31-33 36 39-42 44-48 51 53 54 59 63], 6 on young adults (18-25 years)[35 38 50 55 56 58] and 14 included data on both of these groups[24 25 27 28 30 34 37 43 49 52 57 60-62].

Among studies conducted in the United States, 9 were based on data from the National Study on Drug Use and Health conducted by the Substance Abuse and Mental Health Services Administration (NSDUH https://nsduhweb.rti.org/respweb/homepage.cfm)[29 30 34 37 40-43 52], 7 on data from the Monitoring The Future study based at the University of Michigan (MTFS http://monitoringthefuture.org/)[23 26 35 36 39 48 53], 4 on the Youth Behavioral Risk Surveillance conducted by the Centers for Disease Control and Prevention (YBRS https://www.cdc.gov/healthyyouth/data/yrbs/index.htm)[31-33 47] and 4 on the National Longitudinal Study of Youth conducted by the U.S. Bureau of Labor Statistics (NLSY79 https://www.nlsinfo.org/content/cohorts/nlsy79[24 25], and NLSY97 https://www.nlsinfo.org/content/cohorts/nlsy97[31 38]. Among studies conducted in Australia, 2 were based on the National Drug Strategy Household Survey conducted by the Australian

Institute of Health and Welfare (NDSHS http://data.gov.au/dataset/national-drugs-strategy-household-survey).

Concerning study design, 34 studies were based on repeated cross-sectional data[23 26 27 29-37 39-43 46-59 61-63], 6 on longitudinal cohort data[24 25 38 44 45 60] and one on analyses of routine administrative data[28]. Sample sizes in individual studies ranged from n=336[28] to > 11,703,100[33].

Overall, 16 studies were characterised by a very low risk of bias[29 30 32-34 36 39 42 43 47 48 52 53 57 58 62] and 9 by a low risk of bias[24 25 28 45 46 49-51 54]; in our systematic review only the results of these investigations were analysed.

Decriminalisation of cannabis use (Table 1)

Among the 13 studies examining the consequences of cannabis decriminalisation, three were characterised by a very low risk of bias[57 58 62]. Two of these - one based in Australia (n=15,468) and the second in the Czech Republic (n=1524), and both conducted among adolescents and young adults, found no evidence of statistically significant changes in patterns of cannabis use following policy change[57 62]. However, one study - based in Australia and conducted exclusively among adolescents aged 12-17 years (n=39,0387) - observed a 12% increase in use following cannabis decriminalisation[58]. We also identified one study characterised by a low risk of bias[24] - conducted in the United States and focusing on 14-21 year olds (n=12,686) - which observed no statistically significant effect of cannabis decriminalisation on youths' use.

Meta-analysing all 13 studies, we observed an I^2 of 99.5%, indicating high heterogeneity (Supplementary Figures 1A & 1B). After excluding studies conducted by Williams & Bretteville-Jensen[58] and Miech et al.[35], which appeared to be outliers, the I^2 was reduced to 99.1%, but remained too high to conduct a robust meta-analysis. This was

unchanged when the analysis was restricted to cohort study data, study year (< or >= 2000), a particular age group (12-17 or 18-25 years), or recent cannabis use (30 days).

Legalisation of cannabis use for medical purposes (Table 2)

Twenty studies examined the consequences of the legalisation of cannabis use for medical purposes in the United States from 1996 onwards. Twelve were characterised by a very low risk of bias[29 30 32-34 36 39 42 43 47 52 53]. Of those, six were based on NSDUH data[29 30 34 42 43 52], three on the YRBS[32 33 47] and three on the MTFS[36 39 53]. Altogether six studies (n ranging from 11,453 to 11,703,100) - all conducted among adolescents - one additionally including youths aged 18-20 years[34] and one additionally including youths aged 18-25 years[43] - found no statistically significant effect of the introduction of medical cannabis laws[32-34 36 42 43]. Three of these studies were based on NSDUH data[34 42 43] and two on the YRBS[32 33]. Importantly, both the NSDUH and the YRBS being repeated cross-sectional surveys, the analytical methods used vary across reports in terms of length of follow-up after policy change (from 1 to 9 years), statistical methods (logistic regression[43], difference-in-differences[33], fixed-effects models[34]), as well as covariates. Still, all studies characterised by a very low risk of bias are adjusted for individual demographic characteristics (age, sex, race) as well as contextual factors (at minima a state identifier and the level of cannabis use prior to policy change). In three studies conducted among adolescents, the legalisation of medical cannabis was followed by a decrease in use[30 39 47]. These three reports were based on different large datasets (NSDUH[30], MTFS[39] and YRBS[47], with ns ranging from 11,813 to 973,089). Finally, three studies (ns ranging from 11,813 to 973,089) observed an increase in levels of cannabis use among adolescents (under 18 years) living in a state which passed medical cannabis laws[29 52 53] and one of these observed a similar effect among young adults (ages 18-25 years)[52].

Two studies were characterised by a low risk of bias[28 51]. One, based on routine data (Arrestee Drug Abuse Monitoring system – ADAM, n=336), showed no statistically significant differences in the prevalence of cannabis use (as ascertained by urine tests) among persons seen in hospital emergency departments before and after medical cannabis laws[28]. The second study reported that among cannabis users recruited via social media (n=2,630), the level of cannabis vaping and eating varied with the time since legalisation of medical cannabis – the longer the time since legalisation, the higher the likelihood of use[51].

Importantly, these data indicate that the provisions of laws enabling access to cannabis for medical purposes, such as the amount of cannabis that individuals are allowed to possess and use, the existence of patient registries[47], the proportion of dispensaries per inhabitant, the authorisation of home cultivation, or concomitant laws making it legal to use cannabis for recreational purposes[51] are influential and should be systematically reported by researchers examining the effects of cannabis policies.

Meta-analysing all 20 studies, we observed an I^2 of 100%, indicating high heterogeneity (Supplementary Figures 2A & 2B). After excluding the studies conducted by Wen et al.[34] and Harper et al.[30], which appeared to be outliers, the I^2 was reduced to 98.6%, but remained too high to conduct a robust meta-analysis. This was unchanged when the analysis was restricted to cohort studies, study year (< or >= 2000), a particular age group (12-17 or 18-25 years), or recent cannabis use (30 days).

Legalisation of cannabis for recreational purposes (Table 3)

We identified 8 studies examining the impact of recreational cannabis laws, which make it legal to use and possess small amounts of cannabis, on youths. They were all conducted in the United States, where several states have introduced this form of cannabis legalisation

since 2012. Four studies were based in Washington state[44 45 46 50], two in Colorado[55 64], one in Washington state and Colorado[48] and one in Oregon[49]. Only one study - based on the MTFS - was characterised by a very low risk of bias[48]. This investigation (n=253,902) reported a statistically significant increase in cannabis use among adolescents living in Washington state (3.2% increase among 8th graders and 5.0% increase among 10th graders), but not among those living in Colorado.

We also identified two studies characterised by a low risk of bias. One (n=13,335) reported a 2.0-3.5% increase in the frequency of cannabis use among college students living in Washington state[50] and the other an increase of .02% among middle and high school students living in Colorado (n=24,171)[64].

Meta-analysing all 8 studies, we observed an I^2 of 89.8%, indicating high heterogeneity (Supplementary Figures 3A & 3B). After excluding the study conducted by Cerda et al.[48], which appeared to be an outlier, the I^2 was reduced to 64.4%. This analysis yielded an average standardised mean difference of 0.03 (95% CI -0.01-0.07), suggesting a possible small increase in the use of cannabis following the legalisation of recreational cannabis.

Discussion

Main findings

Our systematic review of studies examining the impact of the liberalisation of cannabis legislation on patterns of use among adolescents and young people, identified 41 reports published prior to March 2018, 16 characterised by a very low risk of bias and 9 by a low risk of bias. With the exception of one study, high quality reports examining the impact of cannabis decriminalisation (n=4) show no statistically significant change in youths' patterns

of use. Similarly, the legalisation of cannabis use for medical purposes, extensively evaluated in the United States, does not appear to have an effect: 6 studies suggest no change in cannabis use among youths, 3 studies observe a decrease, and 4 studies report an increase. However, the legalisation of cannabis for recreational purposes, examined in 6 studies with a very low or low risk of bias, may be associated with a small increase in levels of use among youths.

Overall, policies regarding cannabis use and possession seem to have little effect on actual patterns of use among young people, with the possible exception of the legalisation of recreational use. To date, evidence regarding the impact of the legalisation of recreational cannabis comes from the United States, where prevalence levels of substance use are high and laws liberalising cannabis use tend to be market-oriented. Additional data from other settings (e.g. Uruguay, Canada) will help gain a better understanding of relations between cannabis policy and patterns of use in the population.

Limitations and strengths

Our systematic review has limitations which need to be acknowledged. First, the specific provisions of laws and policies regulating cannabis and which can influence actual access to the substance[2], vary across settings. For example, decriminalisation can imply different limits on the amount of cannabis that leads to a fine – e.g. the possession of 15 g of herb or 5 g of resin in the Czech Republic is fined approximately 550 euros[62]; in the Australian Capital Territory (Canberra region) the possession of up to 25 g is fined approximately 100 euros, while in Western Australia (Perth region) the possession of less than 10 g is tolerated but higher quantities can result in a conviction[65]. Similarly, laws allowing the use and possession of cannabis for medical purposes, currently in place in approximately 20 countries (e.g. Australia, Belgium, Spain, Canada and some states in the

United States) take different forms. For instance, only the Netherlands and some US states make it possible for individuals to purchase or grow cannabis that can be smoked – in other settings individuals have to purchase specific medicines derived from cannabinoids (e.g. the United Kingdom). The legal age at which individuals are authorised to possess cannabis (18 or 21 years) varies across settings, with possibly differential effects on levels of use among young adults. Finally, the price of cannabis, which influences levels of use among young people[57 66], varies from place to place and over time. Clearly, differences in specific policy provisions, which have an impact on cannabis availability, make it difficult to compare different settings. Nevertheless, at the time of its implementation or even before if there is wide media coverage, policy change in and of itself can influence the perceptions of cannabis, which in turn shape levels of use[39], justifying the conduct of this systematic review. Second, the duration of follow-up varies across studies, in part because changes in cannabis policy occurred in different periods and places. This is especially a concern for reports evaluating the impact of recreational cannabis laws: policy changes introduced decades ago (e.g. the Netherlands) were not fully evaluated, while follow-up is limited for more recent policy modifications (e.g. the United States, Uruguay). It is unclear whether the introduction of policies that liberalise cannabis use and possession is most likely to influence patterns of use in the short or in the long-term; in the present report we considered that a follow-up period of at least one year following actual policy implementation was necessary to test a possible effect. Third, among studies examining the consequences of the legalisation of cannabis for recreational purposes, we only identified one study characterised by a very low risk of bias and 5 by a low risk of bias, and the findings we report will need to be confirmed. Finally, our attempt to meta-analyse the results of different studies included in this review

proved inconclusive, with the exception of legalisation of cannabis for recreational purposes: this calls for additional, methodologically robust, studies in this area.

Despite these limitations, our study has several strengths: a) the evaluation of studies published in different disciplines (public health, epidemiology, economics, social policy) through multiple databases; b) the combination of data from different settings (United States, Australia, Europe); c) special attention to the risk of bias, examined using a framework especially developed for observational studies. Moreover, our systematic review takes into consideration different forms of liberalisation of cannabis policies (decriminalisation, legalisation for medical purposes and for recreational purposes), attempting to tackle this complex issue in a thorough way.

Methodological issues

The studies included in this systematic review relied on several different datasets and applied quite varied methods (logistic regression[43], difference-in-differences[33], fixed-effects models [34]), to isolate the effects of policy change on patterns of cannabis use independently of individual and contextual characteristics; such triangulation of different methods is considered especially reliable when, as in this case, it yields consistent results[67]. Importantly, because cannabis policy changes most often occur in settings where public support and levels of use are high, it is essential to take into account levels of cannabis use prior to policy change, as was the case in all reports we considered to present a very low or low risk of bias. Finally, it is important to note that we evaluated relative changes in cannabis use post vs. pre policy change. Levels of cannabis use vary widely across settings and in some places may have been so high prior to policy change that additional increases are unlikely (this may be the case of Colorado where over 25% of 12th graders use cannabis on a monthly basis)[48].

Most studies included in our systematic review were cross-sectional, because reports based on longitudinal data are less numerous and were not always of sufficiently high quality. While repeated cross-sectional studies are well-suited to examine long-term changes in patterns of cannabis use in relation to changes in the legal context, additional evidence from longitudinal data following young people would make it possible to take into account individual characteristics and further strengthen the inference that can be drawn regarding the impact of cannabis policy change.

Implications

Summarising the available evidence, we found that, contrary to what has been observed in adults[34 57 68], cannabis decriminalisation and legalisation for medical purposes are probably not related to significant changes in patterns of use among adolescents and young people. This was also recently reported by a systematic review and meta-analysis which focused on medical cannabis laws and patterns of use in the preceding 30 days among adolescents[69]. On the other hand, the legalisation of cannabis use for recreational purposes may lead to higher levels of use in this age group and a younger age at initiation. Several hypotheses have been proposed to explain this multifactorial phenomenon: a) changes in the reporting of cannabis use; b) a decrease in perceived harmfulness[39]; c) an increase in cannabis availability and access; d) a decrease in price (in legal outlets or on the black market)[70]. While the liberalisation of cannabis policy can have both collective and individual benefits (e.g. decrease in costs of law enforcement, increase in quality control, reduction in individuals' difficulties with the legal system), these data suggest the possibility of small negative public health implications. Adolescents and young adults are especially vulnerable to the consequences of cannabis use, in terms of both biological and social development[71 72], therefore policies that involve the legalisation of recreational use of cannabis need to be

accompanied by prevention efforts targeted towards young people. The most effective prevention programs aim to improve school climate and strengthen youths' psychosocial skills such as self-esteem and conflict resolution[73 74].

Conclusion

In recent decades, cannabis policies have been liberalised in different ways (decriminalisation, legalisation of use for medical or recreational purposes) and in various settings. Our systematic review and meta-analysis of 41 research articles published across disciplines (epidemiology, economics, social policy) and using a variety of datasets and statistical methods shows that cannabis decriminalisation or legalisation of use for medical purposes do not result in higher levels of use among youths. However, legalisation of use for recreational purposes may result in a small increase – it will be important to reassess whether this tendency persists over time, varies across subgroups of youths (male vs. female, urban vs. rural, socioeconomically disadvantaged vs. favoured), and is comparable across settings, particularly as additional countries introduce changes in cannabis policy (e.g. Canada).

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Table 1. Studies examining cannabis use levels in adolescents before and after decriminalisation of cannabis possession (1981-2017).

	Study	Setting	Type of policy change/study period	Inclusion criteria/ n	Study design	Cannabis use measures	Statistical methods/ covariates	Key findings/effect size	Risk of bias
1	Johnston et al., 1981[23]	California, Maine, Minnesota, Ohio (early change) + North Carolina, New York, Missouri (late change) vs. states with no decriminalisation	Decriminalisation of cannabis possession in 1975 and 1976	12th grade students participating in the Monitoring the Future surveys (MTFS)/ n~99,000 per year	Cross-sectional survey (1975-1980)	12 months, 30 day, and daily use	Comparisons of prevalence rates	12-month use: d=0.06, 95% CI 0.0003; 0.127; 30-day use: d=0.125, 95% CI 0.059; 0.191(unadjusted)	Possible
2	Thies & Register, 1993[24]	Alaska, California, Colorado, Maine, Minnesota, Missouri, Nebraska, New York, North Carolina, Ohio, Oregon	Decriminalisation of cannabis possession 1976-1979	14-21 year olds participating in the National Longitudinal Survey of Youths1979 (NLSY) /n=12,686	Cohort study with follow-up in 1984 and 1988.	30 day use	OLS regression models controlled for sex, race, parental education, own education, income, church attendance, marital status, urban setting; legal context regarding underage drinking	1984: d=0.05, 95% CI -0.02; 0.14; 1988: d=0.06, 95% CI -0.03; 0.16 (unadjusted)	Low
3	McGeorge & Aitken, 1997[56]	Australian Capital Territory vs. Melbourne	Decriminalisation of cannabis possession, use and cultivation in 1992	3rd year university students at Australian National University and Melbourne University /n=903	Cross-sectional survey (1994)	12-month use	Chi-square statistics	d=0.21, 95% -0.02; 0.45 (unadjusted)	Probable
4	MacCoun, 1997[61]	Netherlands	Decriminalisation of cannabis in 1976 followed by legalisation in 1984	16-18 year olds participating in a school-based survey (Trimbos) vs. Youths of the same age in the	Repeated cross-sectional surveys: 1970 to 1996	Lifetime use	Comparison of prevalence rates	Netherlands vs. US: d=-0.23; 95% CI -0.26; -0.19 (unadjusted)	Possible

				US (Monitoring the Future)/ n~115,000					
5	Pacula 1998[25]	Alaska, California, Colorado, Maine, Minnesota, Missouri, Nebraska, New York, North Carolina, Ohio, Oregon	Decriminalisation of cannabis possession 1976-1979	14-21 year olds participating in the National Longitudinal Survey of Youths1979 (NLSY)/n=8,008	Cohort study with follow-up in 1984.	30 day use	Two part model controlled for sex, age, race, number of siblings, urban setting, academic achievement, expected years of schooling, illegal activity; parents' marital status, employment status, alcohol use; legal context regarding alcohol use, crime level, beer and cigarette taxes	d=0.0179, 95% CI -0.038; 0.0008	Low
5	DiNardo & Lemieux 2001[26]	California, Colorado, Maine, Minnesota, Mississippi, Nebraska, New York, North Carolina, Ohio, Oregon	Decriminalisation of cannabis possession 1976-1979	12th grade students participating in the Monitoring the Future surveys (MTF) /n~165,000	Cross-sectional survey (1980-1989)	30 day use	Structural regression model controlled for sex, age, race, parental education, weekly hours of work, income, alcohol use, state-level unemployment and alcohol drinking age	d=-0.08, 95% CI -0.12; -0.05	Possible
7	Williams 2004[57]	Australian Capital Territory, Northern Territory vs. non decriminalising states	Decriminalisation of cannabis possession, use and cultivation between 1988 and 1998	14-25 years , Australian National Drug Strategy Household Survey (NDSHS) /n=15,468	Repeated cross-sectional surveys (1988, 1991, 1993, 1995, 1998)	12-month use	Ordered probit model controlled for sex, age, marital status, dependent children, ethnicity, educational level, employment, capital city residence, decriminalisation	d=0.04, 95% CI -0.102; 0.192	Very low

							regime		
8	Williams & Bretteville-Jensen, 2014[58]	South Australia, Australian Capital Territory, Northern Territory, Western Australia vs. non-decriminalising states	Decriminalisation of cannabis possession, use and cultivation between 1987 and 2004.	20-40 year old lifetime users of cannabis participating in the Australian National Drug Strategy Household Survey (NDSHS) /n=39,087	Repeated cross-sectional surveys (1998, 2001, 2004, 2007, 2010)	Age at initiation	Difference-in-differences with discrete time hazard model controlled for sex, education, ethnicity, capital city residence, survey year	12-17 years: d=0.57, 95% CI 0.52; 0.63	Very low
9	Fuller, 2014[59]	England	Declassification of cannabis from schedule B to schedule C drug (2004) and then back (2009)	11-15 year olds participating in a representative school survey/n=6,173	Repeated cross-sectional surveys (2001-2014)	12-month use	Prevalence rates	2004 vs. 2009: d=-0.22, 95% CI -0.29; -0.165 (unadjusted)	Probable
10	Braakmann & Jones, 2014[60]	United Kingdom	Declassification of cannabis from schedule B to schedule C drug (2004)	15-25 year olds participating in the Offending, Crime and Justice Survey (OCJS)/n=2,539	Cohort study (2003-2006)	12-month and 30-day use;	Difference-in-differences model controlled for age and calendar year	12-month use; 15-17 yrs: d=-0.01, 95% CI -0.07; 0.002; 18-25 yrs: d=-0.05, 95% CI -0.15; 0.05; 30-day use: 15-17 years: -0.006, 95% CI -0.009; 0.08; 18-20 years: -0.13, 95% CI -0.24; -0.02	Possible
11	Miech et al, 2015[35]	California vs. other US states	Decriminalisation in 2010	8th, 10th and 12th grade students participating in the Monitoring the Future surveys (MTF)/n=97,238	Repeated cross-sectional surveys (2007-2012)	12-month and 30-day use	GEE regression models	12-month: d=0.32, 95% CI 0.31-0.34; 30-day use: d=0.57, 95% CI 0.55-0.59 (unadjusted)	Possible
12	Shi et al, 2015[63]	Cross-national study of 38 countries	Depenalisation, decriminalisation, and partial prohibition changed since 0-5 years, 5-10 years or >10 years	15 year olds participating in the Health Behaviour in School-Aged Children Study (HBSC)/	Repeated cross-sectional surveys (2001/2002, 2005/2006, 2009/2010)	12-month and regular (>=40 times in lifetime) use	Multilevel logistic random intercept regression	12-month use: d=-0.004, 95% CI -0.02; 0.13; regular use: d=0.17, 95% CI 0.13; 0.20	Possible

				n=172,894					
13	Červený J et al, 2017[62]	The Czech Republic	Decriminalisation of cannabis possession in 2010	15-25 years participating in drug use monitoring surveys/ n=1086 in 2008 and 438 in 2012	Repeated cross-sectional surveys (2008-2012)	Age at initiation	Mixed proportional hazards controlled for sex, education, birth cohort and region of residence	d=-0.26, 95% CI -0.37; -0.15 (unadjusted)	Very low

Table 2. Studies examining cannabis use levels in adolescents before and after the legalisation of cannabis use for medical purposes (1996-2018).

	Study	Setting	Type of policy change/study period	Inclusion criteria/ n	Study design	Cannabis use measure	Statistical methods/ covariates	Key findings/effect size	Risk of bias
1	Khatapoush & Hallfors, 2004[27]	California (CA)	State-level Medical marijuana laws (MML): Proposition 215 (1996)	16-25 year olds participating in the Robert Wood Johnson Foundation's Fighting Back initiative (FB)/n=2,651	Repeated cross-sectional surveys in 1995, 1997 and 1999.	12-month and 30-day use	Logistic regression model	12-month use: d=0.54, 95% CI 0.48; 0.59; 30-month use: d=0.72, 95% CI 0.64; 0.79 (unadjusted)	Probable
2	Gorman et al, 2007[28]	Los Angeles, San Diego, San Jose (CA), Portland (OR)	State-level Medical marijuana laws (MML) introduced before 2002	10-18 year olds registered in the Arrestee Drug Abuse Monitoring system (ADAM)/ on average n=255 in California & n=81 in Oregon	Routine data collection (1995-2002)	Urine test data (>=50 ng of THC per decilitre)	Interrupted time series design	California: 10-18 yrs: d=-0.42, 95% CI -0.60; -0.24; Oregon: 10-18 yrs: d=-0.75, 95% CI -1.33; -0.17 (unadjusted)	Low
3	Wall et al, 2011[29]	Alaska, California, Colorado, Hawaii, Maine, Nevada, Oregon, Washington + Michigan, Montana, New Mexico, Rhode Island, Vermont + Arizona, Delaware, New Jersey vs. other US states	State-level Medical marijuana laws (MML) introduced before 2002	12-17 olds participating in the National Survey of Drug Use and Health (NSDUH)/ n~11,813	Repeated cross-sectional surveys (2002-2008)	30-day use	Fixed effects model with random intercept, controlled for cannabis use 2002-2008	2002-2003: d=0.15, 95% CI 0.07; 0.23	Very low
4	Harper et al, 2012[30]	Alaska, California, Colorado, Hawaii, Maine, Nevada, Oregon,	State-level Medical marijuana laws (MML)	12-17 year olds and 18-25 year olds participating in	Repeated cross-sectional surveys (2002-2009)	30-day use	Difference-in-differences estimates controlled for	12-17 years: d=-1.25, 95% CI –1.29; -1.21; 18-25 years: d=1.71, 95% CI 1.67 - 1.75	Very low

		Washington + Michigan, Montana, New Mexico, Rhode Island, Vermont vs. other US states	introduced before 2002	the National Survey of Drug Use and Health (NSDUH) /n~11,813 per age group			measurement error		
5	Anderson et al, 2012[31]	Alaska, Arizona, California, Colorado, Delaware, District of Columbia, Hawaii, Maine, Michigan, Montana, Nevada, New Jersey, New Mexico, Oregon, Rhode Island, Vermont, Washington vs. other US states	State-level Medical marijuana laws (MML) introduced before 2011	15-19 years olds participating in the National and State Youth Risk Behavior Surveys (YRBS) /n=786,568	Repeated cross-sectional surveys (1993-2011)	30-day use; 30-day frequent use;	Linear regression controlled for age, sex, race, grade, state-level marijuana decriminalisation, BAC 0.08 laws, state beer tax, income per capita, unemployment	YRBS: 30day use: d=-0.32, 95% CI -0.33; -0.32; 30-day frequent use d=-0.18, 95% CI -0.19; -0.18	Possible
6	Lynne-Landsman et al, 2013[32]	Delaware, Michigan, Montana, Rhode Island compared pre and post-MML implementation	State-level Medical marijuana laws (MML) introduced 2003-2009	9-12th graders participating in the Youth Risk Behavior Surveys (YRBS) /n~11,453	Repeated cross-sectional surveys (2003-2009)	30-day use;	Difference in differences controlled for age, ethnicity, and sex	d=0.24, 95% CI 0.20;0.28	Very low
7	Choo et al, 2014[33]	Idaho vs. Montana, Massachusetts vs. Rhode Island, New Hampshire vs. Maine, Utah vs. Nevada, New York vs. Vermont	State-level Medical marijuana laws (MML)	9-12th graders participating in the Youth Risk Behavior Surveys (YRBS)/ n~11,703,100	Repeated cross-sectional surveys since 1991, 1993, 1995, 1997, 1999, 2001, 2003, 2005, 2007	30 day use	Difference-in-differences controlled for state, year, age, sex, race, grade	d=0.065, 95% CI 0.026; 0.105	Very low
8	Wen et al, 2014[34]	District of Columbia, Michigan, Montana, New Jersey, New Mexico, Rhode Island, Vermont vs	State-level Medical marijuana laws (MML) introduced between 2004 and 2010	12-20 year olds participating in the National Survey on Drug Use and Health (NSDUH)/ n~183,600	Repeated cross-sectional surveys (2004-2011)	30-day use;	Fixed-effects models controlled for age, sex, race, self-reported health, cigarette use, urban residence, family	d=-1.72, 95% CI:-1.73;-1.71	Very low

		US states with no MML laws by 2010					poverty, state-level unemployment, mean income, median income, alcohol excise taxes.		
9	Hasin et al, 2015[36]	21 US states that passed MML vs. non-MML US states	State-level Medical marijuana laws (MML) introduced by 2014	8th, 10th and 12th grade (13, 15, 17) students participating in the Monitoring the Future surveys (MTF) /n=1,098,070	Repeated cross-sectional surveys (1991-2014)	30-day use;	Multilevel regression models controlled for sex, age, race, parental education, class size, private school, urban setting, state-level proportion of males, whites, persons with no high school education and aged 11-24 years	d=-0.033, 95% CI -0.039; -0.026	Very low
10	Schuermeyer et al, 2015[37]	Colorado vs. 34 non-MML US states	State-level Medical marijuana laws (MML) introduced in 2009	12-20 year olds participating in the National Survey on Drug Use and Health (NSDUH)/ n~158,600 12-17 year olds + 159,200 18-25 year olds	Repeated cross-sectional surveys (2006-2011)	>=20 times in 30-days use	Logistic regression controlled for state, year, age, sex, race, educational level and state-by-year interaction	12-17 yrs: d=0.09, 95% CI -0.04 ; 0.23; 18-25 yrs: 0.23, 95% CI 0.16-0.29 (unadjusted)	Possible
11	Pacula et al, 2015[38]	Alaska, Arizona, California, Colorado, Delaware, District of Columbia, Hawaii, Maine, Maryland, Michigan, Montana, Nevada, New Jersey, New	State-level Medical marijuana laws (MML) introduced before 2012; comparison of different legal provisions: patient registry; home cultivation;	- <21 year olds participating in the National Longitudinal Survey of Youths1997 (NLSY)/46,375	Cohort study (1997-2011)	30-day use;	Difference-in-differences models controlled for population unemployment rate, age distribution, state beer tax rate, BAC 0.08 tax;	d=-0.0109, 95% CI, -0.03; 0.009	Possible

		Mexico, Oregon, Rhode Island, Vermont, Washington vs. US states with no MML in 2012	legal dispensaries;						
12	Keyes et al, 2016[39]	21 US states that passed MML vs. non-MML US states	State-level Medical marijuana laws (MML) introduced by 2014	8th, 10th and 12th grade (13, 15, 17) students participating in the Monitoring the Future surveys (MTF) /n=973,089	Repeated cross-sectional surveys (1991-2014)	30-day use;	Time-varying multilevel regression models controlled for sex, age, race, parental education, class size, private school, urban setting, state-level proportion of males, whites, persons with no high school education and aged 11-24 years	d=-0.03, 95% CI -0.03;-0.027	Very low
13	Maxwell & Mendelson, 2016[40]	California, Colorado and Washington vs. other US States	State-level Medical marijuana laws (MML) and Recreational marijuana laws (RML)	12-25 year olds participating in the National Survey of Drug Use and Health (NSDUH)	Repeated cross-sectional surveys (2002-2013)	12-month use	Comparison of prevalence rates	Impossible to calculate	Probable
14	Stolzenberg et al, 2016[41]	Alaska, Arizona, California, Colorado, Delaware, Hawaii, Maine, Michigan, Montana, Nevada, New Jersey, New Mexico, Oregon, Rhode Island, Vermont, Washington vs.	State-level Medical marijuana laws (MML) introduced between 1998 and 2011	12-17 olds participating in the National Survey of Drug Use and Health (NSDUH) /n~112,500	Repeated cross-sectional surveys (2002-2011)	30-day use	Random effects model controlled for state-level medical cannabis possession limit, cannabis availability, % enrolled in drug class, alcohol use, prior crime conviction, % families on income	d=0.060, 95% CI 0.034;0.087	Possible

		other US states					assistance, % juveniles who skipped school, % families where the father resides in household, % male, % white		
15	Wall et al, 2016[42]	Arizona, Delaware, Michigan, Montana, New Jersey, New Mexico, Rhode Island, Vermont vs. other US states	State-level Medical marijuana laws (MML) introduced between 2004 and 2011	12-17 olds participating in the National Survey of Drug Use and Health (NSDUH) /n~112,500	Repeated cross-sectional surveys (2002-2011)	30-day use	Fixed effects model	d=-0.0059, 95% CI -0.030;0.018	Very low
16	Martins SS et al, 2016[43]	Arizona, Connecticut, Delaware, Illinois, Massachusetts, Michigan, New Hampshire, New Jersey, New Mexico, Rhode Island vs. other US states	State-level Medical marijuana laws (MML) introduced between 2005 and 2013	12-17 and 18-25 year olds participating in the National Survey of Drug Use and Health (NSDUH)/ n=175,000 12-17 year olds and 175,000 18-25 year-olds	Repeated cross-sectional surveys (2004-2013)	30-day use	Multilevel logistic regression controlled for sex, ethnicity, insurance status, household income, population density, state proportions of sex, ethnicity, youths, education, unemployment, median household income	12-17 yrs: d=0.02, 95% CI -0.04-0.08; 18-25 yrs: d=0.006, 95% CI -0.035 ; 0.047).	Very low
17	Johnson et al, 2017[47]	Alaska, Arizona, Colorado, Delaware, Maine, Michigan, Montana, Nevada, New Jersey, New Mexico, Rhode Island, Vermont vs. other US states	State-level Medical marijuana laws (MML) introduced between 1998 and 2011	9-12th graders (14-17) participating in the Youth Risk Behavior Surveys (YRBS) /n=715,014	Repeated cross-sectional surveys (1991-2011)	30-day use and 30-day heavy use (>=20 times)	Fixed effect multiple logistic regression controlled for year, state, age, sex, ethnicity	30-day use: d=-0.042, 95% CI -0.051;-0.032; 30-day heavy use: d=0.0001, 95% CI -0.018;0.0185	Very low
18	Borodovsky et al, 2017[51]	Alaska, Colorado, District of Columbia, Oregon, Washington vs. 20	Legalisation status: MML or RCCL vs. no legal cannabis law	14-18 year olds recruited online (via targeted Facebook	Cross-sectional survey (April 29-May 18, 2016)	30-day cannabis use via smoking, vaporizing, or	Logistic and linear regression controlled for age, gender, race, grade	d=0.064, 95% CI -0.048;0.176	Low

		US states that did not		invitations) /n=2,630		eating.	level, lifetime days of cannabis use, age of onset.		
19	Mauro et al, 2017[75]	Arizona, Connecticut, Delaware, Illinois, Maine, Michigan, New Hampshire, New Jersey, New Mexico, Rhode Island, vs. 27 US states with no MML by 2013	State-level Medical marijuana laws (MML) introduced prior to 2015	12-17 and 18-25 year olds participating in the National Survey of Drug Use and Health (NSDUH) /n~175,000 12-17 year-olds and 175,000 18-25 year year olds	Repeated cross-sectional surveys (2004-2013)	State-level 30-day and daily use	Multilevel linear regression controlled for trends in marijuana use and state-level % males, % White, % aged 10-24 years, % > 25 yrs with no high school degree, % unemployed, median household income.	30-day use: 12-17 years: d=0.041, 95% CI 0.022; 0.059; 18-25 years: d=0.016, 95% CI 0.003; 0.029; daily use: 12-17 years: d=-0.003, 95% CI -0.021; 0.014; 18-25 years: d=0.064, 95% CI 0.050; 0.078	Very low
20	Cerda et al, 2018[10]	Arizona, California, Colorado, Connecticut, Delaware, Illinois, Maine, Maryland, Massachusetts, Michigan, Minnesota, Montana, Nevada, New Hampshire, New Jersey, New Mexico, New York, Oregon, Rhode Island, Vermont, Washington vs. other US states	State-level Medical marijuana laws (MML) introduced prior to 2015; time since legalisation.	8th, 10th and 12th graders (13, 15, 17) participating in the Monitoring the Future Survey/ n=1,140,768	Repeated cross-sectional survey (1991-2015)	30-day use	Difference-in-differences models controlled for individual grade, age, sex, race/ethnicity, socioeconomic status, number of students per grade, public vs. private school, school in metropolitan statistical area, state-level % males, % White, % aged 10-24 years, and % older than 25 with no high school degree.	d=0.0176, 95% CI 0.0170;0.0182	Very low

Table 3. Studies examining cannabis use levels in adolescents before and after legalisation of recreational cannabis use (2016-2018).

	Study	Setting	Type of policy change/study period	Inclusion criteria/ n	Study design	Cannabis use measures	Statistical methods/ covariates	Key findings	Risk of bias
1	Estoup et al, 2016[44]	Washington	Legalisation in 2012	High school students (14-17) with problematic substance use enrolled in high school in the Seattle area/ n=262	Cohort study (2010-2015)	3-month use	Mediation model	d=0.061, 95% CI -0.110; 0.232 (unadjusted)	Possible
2	Mason et al, 2016[45]	Washington vs. other US states	Legalisation in 2012	8th graders (14) in Tacoma, WA participating in a longitudinal study/n=238	Cohort study (2010/2011-2012/2013)	30-day use	Multilevel regression models controlled for substance use initiation prior to baseline	d=0.323, 95% CI -0.177; 0.825	Low
3	Fleming et al, 2016[46]	Washington vs. other US states	Legalisation in 2012	10th (16) graders participating in the biennial Washington state school survey/n=30,365	Repeated cross-sectional surveys (2000-2014)	30-day use	Logistic regression analyses controlled for perceived harm of marijuana, alcohol use, and year	d=0.044, 95% CI -0.019; 0.069	Low
4	Cerdá et al, 2017[48]	Colorado and Washington vs. other US states	Legalisation in 2012	13-18 years participating in the Monitoring the Future surveys (MTF)/ n= 253,902	Repeated cross-sectional surveys (2010-2015)	30-day use	Difference-in-differences	d=1.03, 95% CI 1.00; 1.06	Very low
5	Kerr et al, 2017[49]	2 universities in Oregon vs. 6 in other US states	Legalisation in 2015	18-26 year old college undergraduates participating in the Healthy Minds Study/n=10,924	Repeated cross-sectional surveys (2014 and 2016)	30-day use	Mixed-effects logistic regression controlled for cigarette use, year in college, age, sex, race, residential type, relationship status, sexual	d=0.0139, 95% CI 0.048; 0.075	Low

							orientation, international student status, depression, anxiety, adjustment, institution size and survey period		
6	Miller et al, 2017[50]	Washington	Legalisation in 2012; Opening of licensed retail stores for marijuana in 2014	College students participating in the National College Health Assessment (WSU NCHA)/n=13,335	Repeated cross-sectional surveys (2005, 2006, 2008, 2010, 2012, 2014, 2015)	30-day use	Logistic regression controlled for age, sex, race, year in school, estimated secular increase in cannabis use.	Post MML (2014): d=0.04, 95% CI 0.002 ; 0.083; post-RML (2015): d=0.082, 95% CI 0.034 ; 0.130	Low
7	Harpin et al, 2018[64]	Colorado	Legalisation in 2012	6-12th grade (11-17) students (Healthy Kids Colorado Survey)/n=24,171	Repeated cross-sectional survey (2013 and 2014)	30-day use	Comparison of prevalence rates	d=0.006, 95% CI -0.026; 0.038 (unadjusted)	Low
8	Jones et al., 2018[55]	Colorado	Legalisation in 2012	College students(22-24 years) n=1,413	Repeated cross-sectional survey (October 2013, March 2014, October 2014 and March 2015)	Lifetime	Comparison of prevalence rates	d=-0.215, 95% CI -0.385; -0.039 (unadjusted)	High

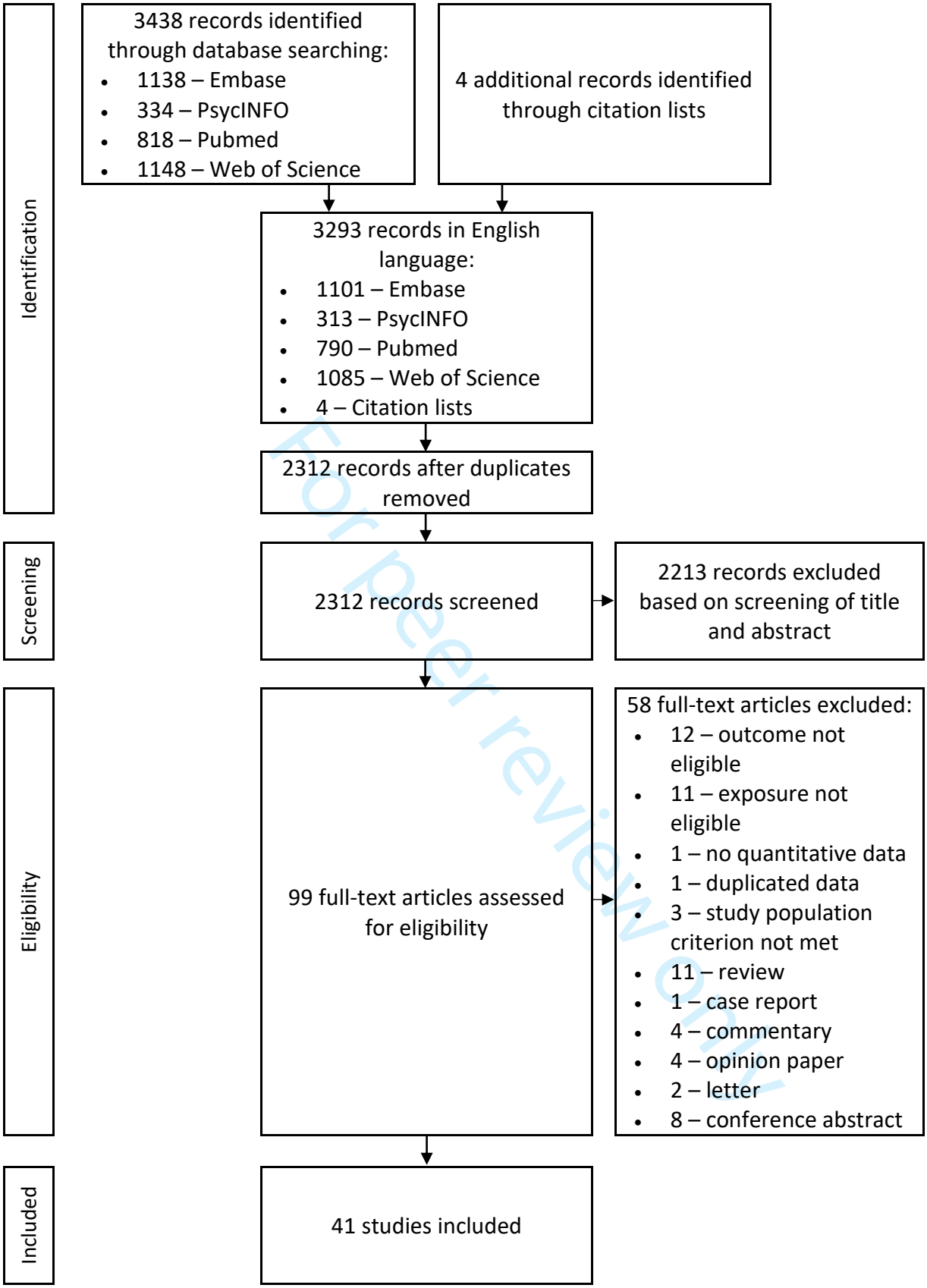
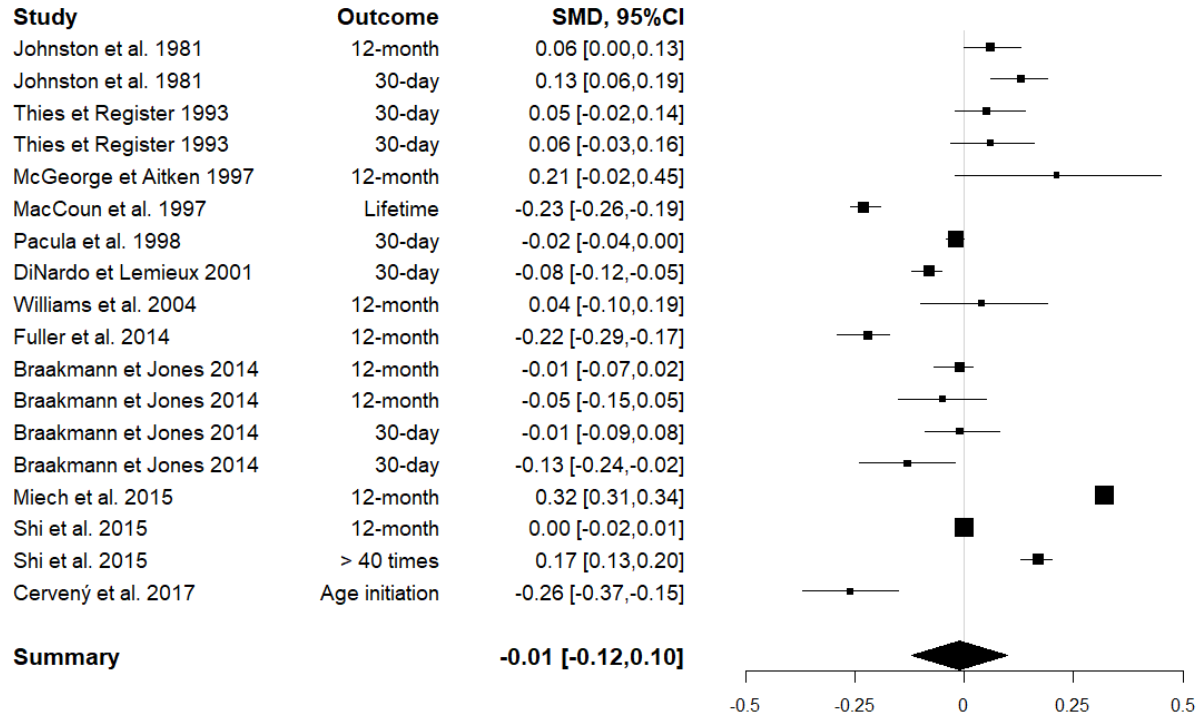
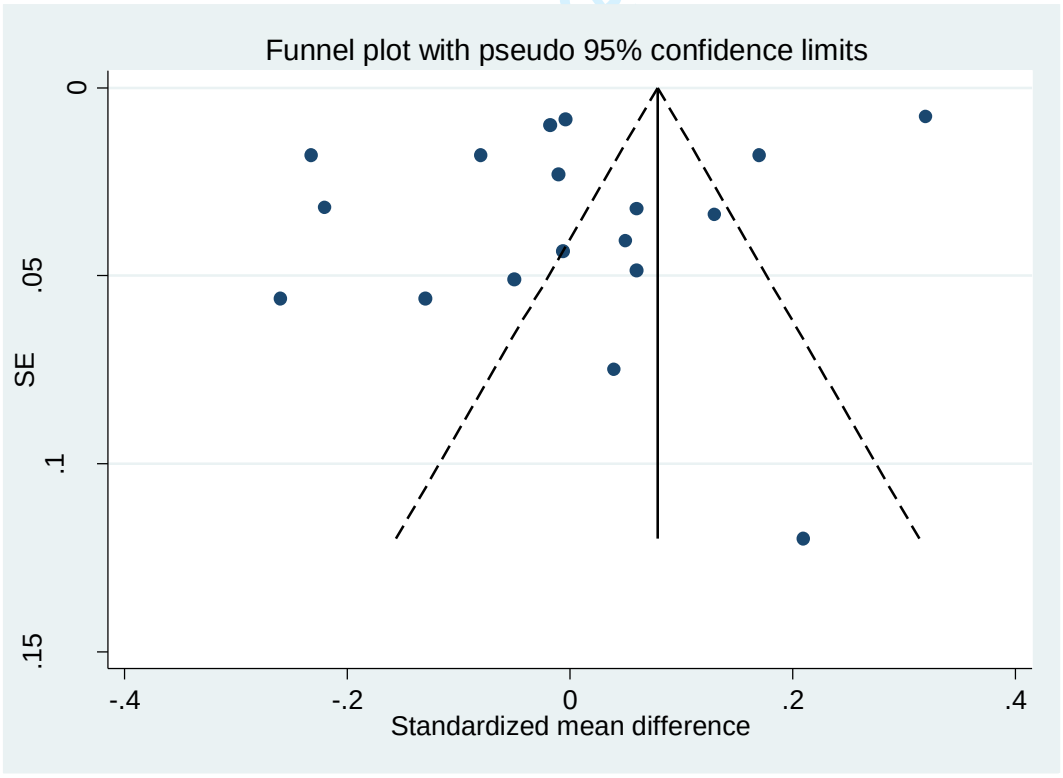


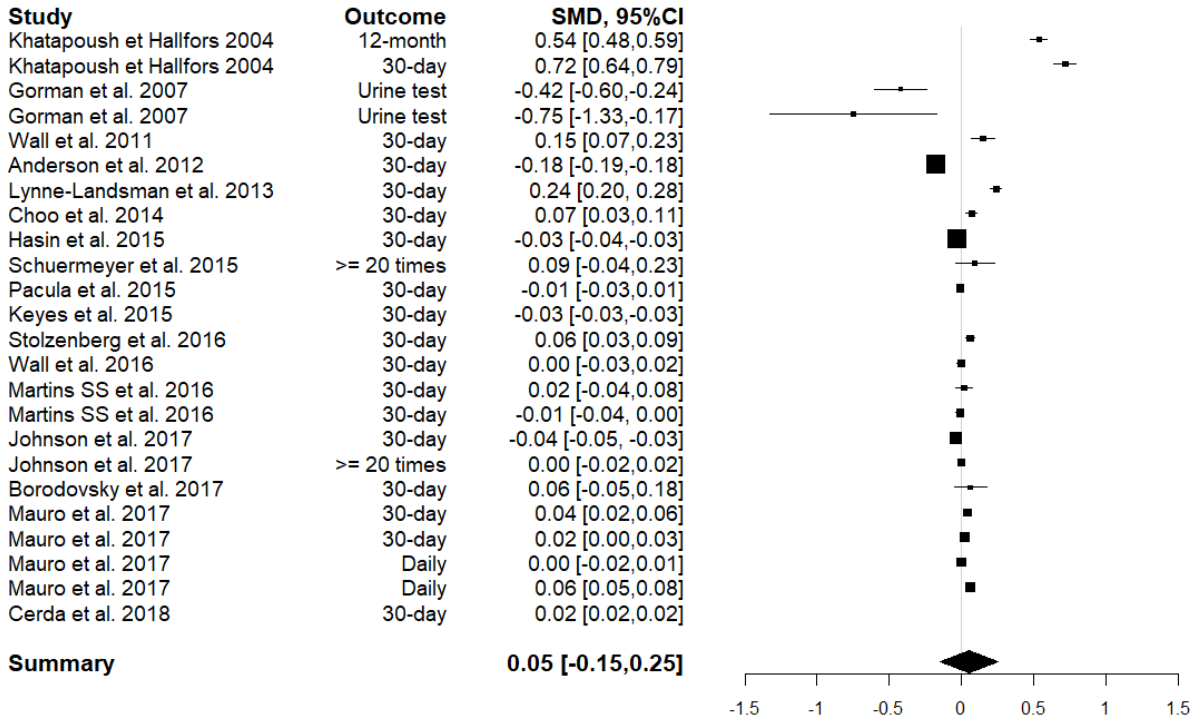
Figure 1. Flowchart showing the screening and selection process of articles selected for the study of the impact of liberalisation of cannabis policy with regard to levels of use in adolescents and young adults.



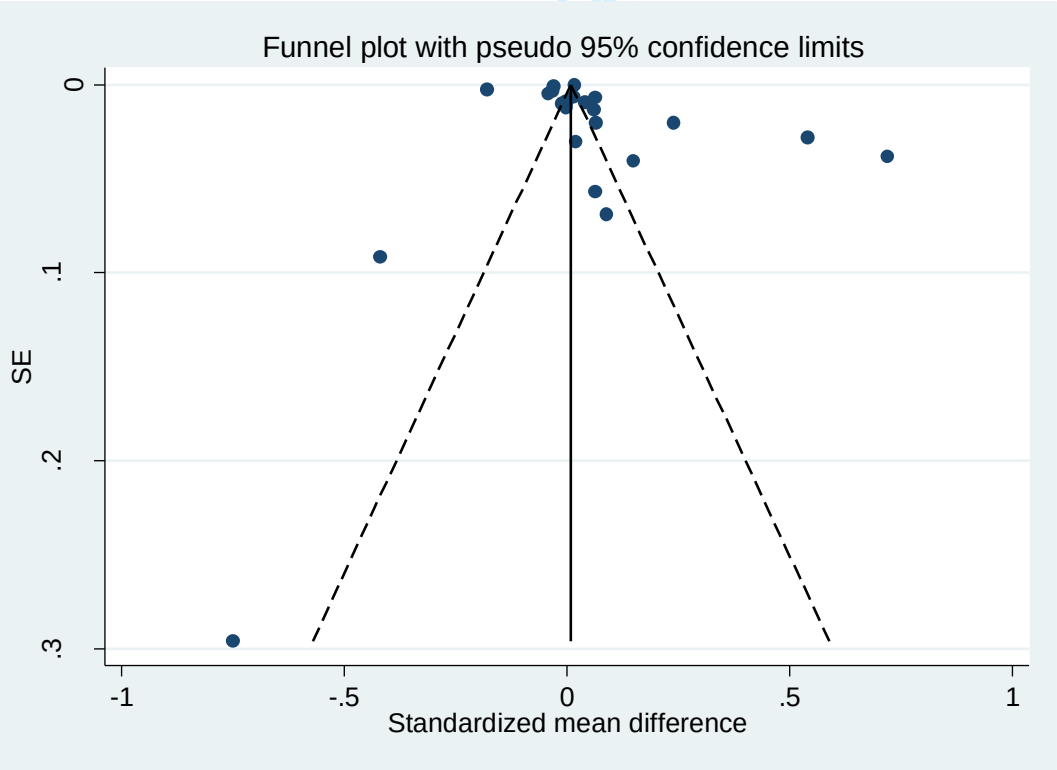
Supplementary Figure 1A : Meta-analysis of studies examining the relationship between cannabis decriminalization and levels of use in adolescents and young adults (12-25 years, prior to March 2018).



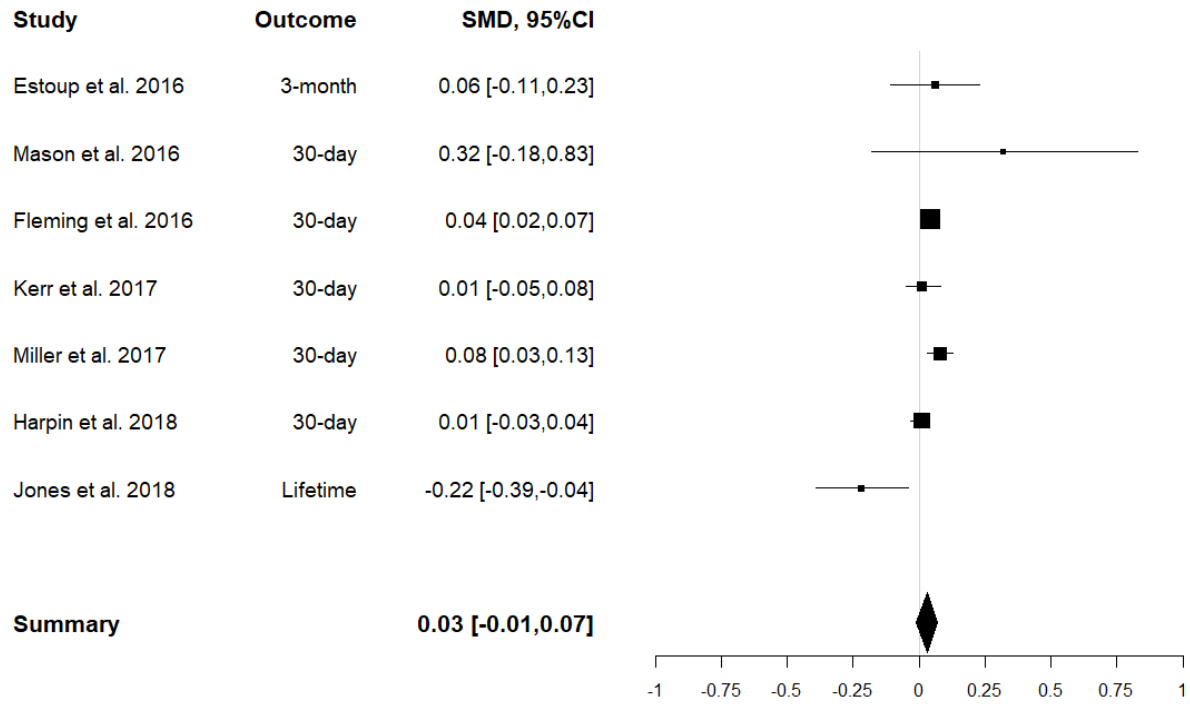
Supplementary Figure 1B : Funnel plot of studies examining the relationship between cannabis decriminalisation and levels of use in adolescents and young adults (12-25 years, prior to March 2018).



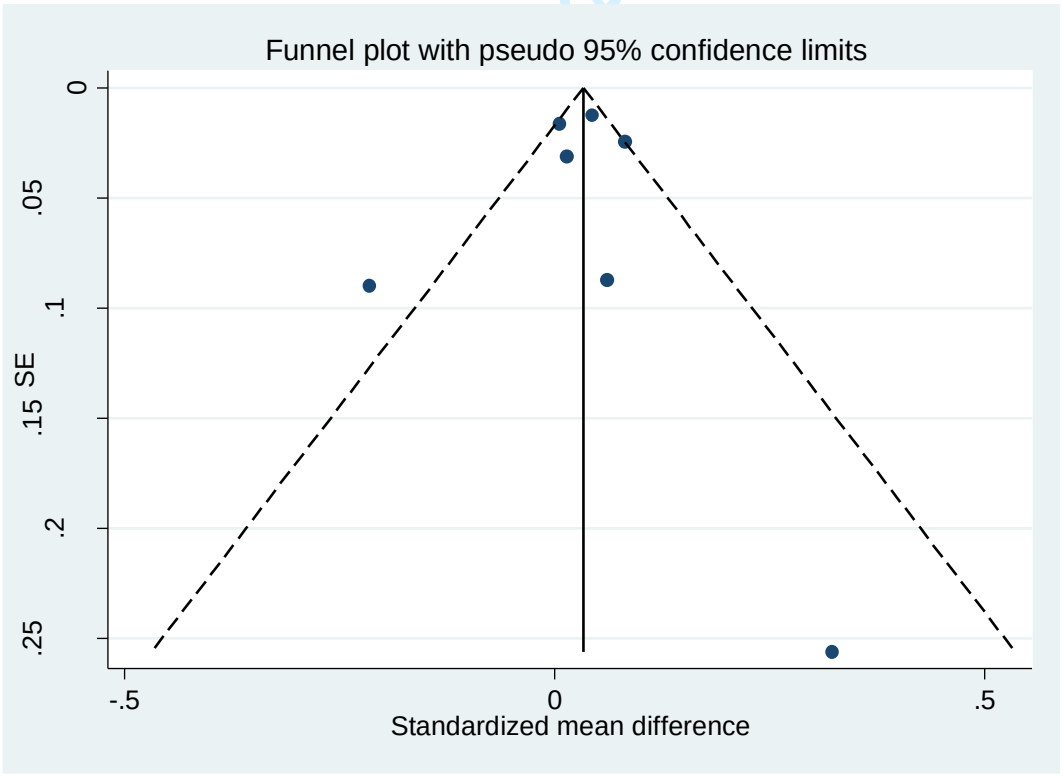
Supplementary Figure 2A : Meta-analysis of studies examining the relationship between the legalisation of cannabis for medical purposes and levels of use in adolescents and young adults (12-25 years, prior to March 2018).



Supplementary Figure 2B : Funnel plot of studies examining the relationship between legalisation of cannabis for medical purposes and levels of use in adolescents and young adults (12-25 years, prior to March 2018).



Supplementary Figure 3A : Meta-analysis of studies examining the relationship between the legalisation of cannabis for recreational purposes and levels of use in adolescents and young adults (12-25 years, prior to March 2018).



Supplementary Figure 3B : Funnel plot of studies examining the relationship between legalisation of cannabis for recreational purposes and levels of use in adolescents and young adults (12-25 years, prior to March 2018).

PRISMA-DTA Checklist

Section/topic	#	PRISMA-DTA Checklist Item	Reported on page #
TITLE / ABSTRACT			
Title	1	Identify the report as a systematic review (+/- meta-analysis) of diagnostic test accuracy (DTA) studies.	1 & 2
Abstract	2	Abstract: See PRISMA-DTA for abstracts.	2-3
INTRODUCTION			
Rationale	3	Describe the rationale for the review in the context of what is already known.	5-6
Clinical role of index test	D1	State the scientific and clinical background, including the intended use and clinical role of the index test, and if applicable, the rationale for minimally acceptable test accuracy (or minimum difference in accuracy for comparative design).	6
Objectives	4	Provide an explicit statement of question(s) being addressed in terms of participants, index test(s), and target condition(s).	6
METHODS			
Protocol and registration	5	Indicate if a review protocol exists, if and where it can be accessed (e.g., Web address), and, if available, provide registration information including registration number.	6-8
Eligibility criteria	6	Specify study characteristics (participants, setting, index test(s), reference standard(s), target condition(s), and study design) and report characteristics (e.g., years considered, language, publication status) used as criteria for eligibility, giving rationale.	7-8
Information sources	7	Describe all information sources (e.g., databases with dates of coverage, contact with study authors to identify additional studies) in the search and date last searched.	6-7
Search	8	Present full search strategies for all electronic databases and other sources searched, including any limits used, such that they could be repeated.	6-7
Study selection	9	State the process for selecting studies (i.e., screening, eligibility, included in systematic review, and, if applicable, included in the meta-analysis).	6-7
Data collection process	10	Describe method of data extraction from reports (e.g., piloted forms, independently, in duplicate) and any processes for obtaining and confirming data from investigators.	8
Definitions for data extraction	11	Provide definitions used in data extraction and classifications of target condition(s), index test(s), reference standard(s) and other characteristics (e.g. study design, clinical setting).	8
Risk of bias and applicability	12	Describe methods used for assessing risk of bias in individual studies and concerns regarding the applicability to the review question.	6-7
Diagnostic accuracy measures	13	State the principal diagnostic accuracy measure(s) reported (e.g. sensitivity, specificity) and state the unit of assessment (e.g. per-patient, per-lesion).	N/A
Synthesis of results	14	Describe methods of handling data, combining results of studies and describing variability between studies. This could include, but is not limited to: a) handling of multiple definitions of target condition. b) handling of multiple thresholds of test positivity, c) handling multiple index test readers, d) handling of indeterminate test results, e) grouping and comparing tests, f) handling of different reference standards	8-9

PRISMA-DTA Checklist

Section/topic	#	PRISMA-DTA Checklist Item	Reported on page #
Meta-analysis	D2	Report the statistical methods used for meta-analyses, if performed.	8-9
Additional analyses	16	Describe methods of additional analyses (e.g., sensitivity or subgroup analyses, meta-regression), if done, indicating which were pre-specified.	8-9
RESULTS			
Study selection	17	Provide numbers of studies screened, assessed for eligibility, included in the review (and included in meta-analysis, if applicable) with reasons for exclusions at each stage, ideally with a flow diagram.	9-10
Study characteristics	18	For each included study provide citations and present key characteristics including: a) participant characteristics (presentation, prior testing), b) clinical setting, c) study design, d) target condition definition, e) index test, f) reference standard, g) sample size, h) funding sources	10-11, Tables 1, 2&3
Risk of bias and applicability	19	Present evaluation of risk of bias and concerns regarding applicability for each study.	11-14
Results of individual studies	20	For each analysis in each study (e.g. unique combination of index test, reference standard, and positivity threshold) report 2x2 data (TP, FP, FN, TN) with estimates of diagnostic accuracy and confidence intervals, ideally with a forest or receiver operator characteristic (ROC) plot.	N/A
Synthesis of results	21	Describe test accuracy, including variability; if meta-analysis was done, include results and confidence intervals.	11-12; 13; 14
Additional analysis	23	Give results of additional analyses, if done (e.g., sensitivity or subgroup analyses, meta-regression; analysis of index test: failure rates, proportion of inconclusive results, adverse events).	11-12; 13; 14
DISCUSSION			
Summary of evidence	24	Summarize the main findings including the strength of evidence.	14-15
Limitations	25	Discuss limitations from included studies (e.g. risk of bias and concerns regarding applicability) and from the review process (e.g. incomplete retrieval of identified research).	15-17
Conclusions	26	Provide a general interpretation of the results in the context of other evidence. Discuss implications for future research and clinical practice (e.g. the intended use and clinical role of the index test).	18-19
FUNDING			
Funding	27	For the systematic review, describe the sources of funding and other support and the role of the funders.	N/A

Adapted From: McInnes MDF, Moher D, Thombs BD, McGrath TA, Bossuyt PM, The PRISMA-DTA Group (2018). Preferred Reporting Items for a Systematic Review and Meta-analysis of Diagnostic Test Accuracy Studies: The PRISMA-DTA Statement. JAMA. 2018 Jan 23;319(4):388-396. doi: 10.1001/jama.2017.19163.

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BMJ Open

Does liberalisation of cannabis policy influence levels of use in adolescents and young adults? A systematic review and meta-analysis

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Does liberalisation of cannabis policy influence levels of use in adolescents and young adults? A systematic review and meta-analysis

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Does liberalisation of cannabis policy influence levels of use in adolescents and young adults? A systematic review and meta-analysis

Keywords : cannabis, marijuana, decriminalisation, legalisation, epidemiology, adolescents, young adults

Abstract

Objectives: To examine the effect of the introduction of policies liberalising cannabis use and possession (decriminalisation, legalisation) on adolescents' and young adults' levels of use.

Design: Systematic review and meta-analysis.

Data Sources: Pubmed, PsycINFO, Embase and Web of Science were searched through March 1st 2018.

Eligibility Criteria: Original research reports were searched for terms including (law* OR decriminalisation OR legalisation) AND (cannabis OR pot OR weed OR marijuana OR grass) AND (young OR youth OR adolescen* OR teen* OR school* OR student), looked for in MeSH terms and in the text.

Data extraction and synthesis: Two independent readers reviewed the eligibility of titles and abstracts, read eligible articles, and four authors assessed the risk of bias (Quality Assessment Tool for Observational Cohort and Cross-Sectional Studies). Extracted data were meta-analysed. The protocol was registered with PROSPERO (CRD42018083950).

Results: Altogether, 3438 records were identified via search terms and 4 via citation lists; 2312 were retained after removal of duplicates, 99 were assessed for eligibility and 41 original research reports were included in our systematic review. Among them, 13 examined cannabis decriminalisation, 20 legalisation for medical purposes and 8 legalisation for recreational purposes. Findings regarding the consequences of cannabis decriminalisation or legalisation for medical purposes were too heterogeneous to be meta-analysed. Our

systematic review and meta-analysis suggest a small increase in cannabis use among adolescents and young adults following legalisation of cannabis for recreational purposes (standardised mean difference of 0.03, 95% CI -0.01-0.07). Nevertheless, studies characterised by a very low/low risk of bias showed no evidence of changes in cannabis use following policy modifications.

Conclusions: Cannabis policy liberalisation does not appear to result in significant changes in youths' use, with the possible exception of legalisation for recreational purposes which requires monitoring over time.

Strengths and limitations of this study

- To date, this is the first study to attempt to summarise research on the consequences of various types of changes in cannabis laws and policies (decriminalisation as well as different forms of legalisation) with regard to patterns of use among adolescents and young adults.
- The duration of follow-up varied across studies, partly because changes in cannabis policy occurred in different periods and places.
- Among studies examining the consequences of the legalisation of cannabis for recreational purposes, only one was characterised by a very low risk of bias and 5 by a low risk of bias, therefore the findings will need to be confirmed in future research.

Introduction

Cannabis is one of the most frequently used psychoactive substances in North America, Europe, Oceania, and North Africa (12-month prevalence of 3.8% in the world)[1]. Since the 1961 Single Convention on Narcotic Drugs, cannabis is illegal in most countries. However, in the past 20 years a majority of US states (thirty one including the District of Columbia) and several countries (e.g. Spain, Uruguay, Portugal) have liberalised their cannabis legislation by decriminalising or legalising use for medical or recreational purposes[2]. Decriminalisation is the reduction of penalties for cannabis use, while maintaining penalties for cannabis supply. Legalisation is the permission to use and supply oneself (via home growing or controlled sale). Legalisation for medical use is permission to use and sometimes supply with the involvement of a medical professional (e.g. with a doctor's prescription or recommendation)[3].

In many settings - especially where cannabis is widely used – public support for legalisation is widespread[4 5]. For cannabis users, decriminalised or regulated access to the substance decreases the legal and criminal risks incurred. Potential collective benefits of cannabis policy liberalisation include: a) reduced law enforcement costs, b) improvements in the quality of the substance used, c) in case of commercial legalisation, additional tax revenue[6].

Still, cannabis is a source of addiction and can have deleterious health consequences in the short and long-terms, including impairments in memory and concentration[7], risk of injury, or respiratory problems[8]. Moreover, liberalised access to cannabis could also influence the levels of use of other psychoactive substances (e.g. tobacco, alcohol)[9 10]. At the same time, there is also evidence that in the United States, the recent increase in opioid use

is less marked in states which recently implemented policies liberalising cannabis regulations[11].

In adults, the liberalisation of cannabis policy has been followed by increases in levels of heavy cannabis use[12-15]. This may be driven by reductions in the perceived risks[16], price decreases, as well as increases in cannabis availability[13 15]. However, in adolescents, who may be especially vulnerable to the negative consequences of cannabis[7], the impact of policy liberalisation is unclear[13]. As additional US states and European countries are considering liberalising cannabis legislation, there is need to evaluate the potential public health consequences of such policy change.

To gain better understanding of the influence of changes in cannabis policy on patterns of use among adolescents and young adults. Youths are a high risk group in terms of illegal substance use and may be especially sensitive to changes in policy; at the same time they may also be especially vulnerable to the biological, psychological and behavioural consequences of cannabis. Data published before March 1st 2018 on this topic were systematically reviewed and meta-analysed.

Methods

Search strategy

Following PRISMA guidelines[17], we conducted a systematic review of studies testing quantitative differences in cannabis use among adolescents and young adults before and after policy change, published prior to March 1, 2018.

Specifically, the following search terms were introduced in Pubmed, Web of Science, EMBASE, PsycINFO: (law* OR decriminalisation OR legalisation) AND (cannabis OR pot OR weed OR marijuana OR grass) AND (young OR youth OR adolescen* OR teen* OR school* OR student). Searches were specified for both MeSH terms and text words and were modified to

meet the requirements of each database. Only articles in English were identified. All titles and abstracts were independently screened by two of the authors to determine potential eligibility. Full texts of all potentially eligible studies were read by two of the authors (FH, MAdS) and discussed with all other authors in case of disagreement. The protocol was registered in PROSPERO (CRD42018083950) and followed the PRISMA framework[17]. The full search strategy is detailed in Supplementary material (Figure 1).

Inclusion criteria

To be included, studies had to be conducted among individuals younger than 25 years and quantitatively assess whether cannabis policy change (defined as decriminalisation, or legalisation of cannabis use for medical or recreational purposes) as compared to no change or the situation prior to change, was associated with changes in cannabis use. This age limit was selected as it is a meaningful cut-off for the potentially negative biological and social effects of cannabis[7] as well as a frequently-used upper bound to define young people. We excluded articles: a) exclusively based on participants older than 25 years; b) only reporting changes in perceptions of cannabis use; c) not including at least two measures of cannabis use and which did not make it possible to compare changes between before and after policy change; d) not including quantitative data; e) reviews, letters, opinions and policy papers.

Patient and public involvement

This research was based on analyses of previously published studies and did not involve direct patient involvement.

Risk of bias

In order to judge the quality of studies that were analysed, risk of bias was assessed using the Quality Assessment Tool for Observational Cohort and Cross-Sectional Studies developed by the National Institute of Health (NIH) (https://www.nhlbi.nih.gov/health-

pro/guidelines/in-develop/cardiovascular-risk-reduction/tools/cohort). Two independent raters evaluated each study on up to 11 items including characteristics of the study population, exposure and outcome measurement, time frame adequacy, loss to follow-up (cohort studies; <20% being considered as associated with low bias), adjustment for confounders. This yielded a rating of very low, low, possible or probable risk of bias for each study. Studies defined as presenting a very low risk of bias had no identified flaws. Studies characterised by a low risk of bias provided insufficient information regarding the study time frame or loss to follow-up (where applicable). Studies considered to present a possible risk of bias were characterised by any of the following: a) insufficient information about the study population recruitment or follow-up (where applicable), b) insufficient definition of exposure or outcome, c) a study period of < 1 year between exposure and outcome, or d) insufficient adjustment for potentially confounding individual or contextual factors. Studies considered to present a probable risk of bias were characterised by two or more of the risks identified above. Differences in ratings between coders were discussed in joint meetings.

Data extraction

A coding sheet was developed to identify: study authors, place of study, type of policy change/ study period, participant characteristics (ns), study design, cannabis use measure, statistical methods used/covariates controlled for, key findings and risk of bias.

Meta-analysis

To meta-analyse the effects of the liberalisation of cannabis policy on levels of use, we calculated Standardised Mean Differences (SMD) and associated 95% confidence intervals for each finding using the Practical Meta-Analysis Effect Size Calculator[18]. Effects sizes from different studies were combined into a weighted mean effect size. Each effect size was weighted by the inverse of its variance and then averaged[19]. Standard meta-analytical

procedures suppose the independence of effects[20]. However, several primary studies provided multiple correlated effect size estimates for the same underlying outcome (e.g. 30-day use, 12-month use etc.). To avoid the loss of information resulting from the selection of only one effect size per study, we used the Robust Variance Estimation (RVE) method[21], which makes it possible to handle statistically dependent effect sizes. A fixed effect meta-analysis was undertaken in the absence of significant heterogeneity, otherwise a random effects model was used [22]. To test for homogeneity, we computed the Q statistic to determine whether each set of effect sizes shared a common population effect size[19]. To interpret between-study heterogeneity, we used the I^2 statistic; an I^2 <= 50% is generally considered to indicate low heterogeneity[23].

To study whether cannabis use in adolescents and young adults varied as a function of 1) cannabis decriminalisation, 2) legalisation of cannabis use for medical purposes or 3) legalisation of cannabis use for recreational purposes, we conducted three main meta-analyses.

For each type of cannabis policy change, we also performed a priori hypothesised subgroup analyses, according to study design (cohort vs. cross-sectional), study year (< 2000 vs. ≥ 2000), participants' age (< vs. ≥ 18 years) and the measure of cannabis use (30-day use vs. 12-month use). Studies included in this review did not present stratified results based on whether participants were < vs. ≥ 21 years (the legal age for cannabis use in US states which legalised the substance), making it impossible for us to conduct sensitivity analyses using this age cut-off.

Finally, because the results of a meta-analysis can be biased by studies with non-significant results being less likely to be published, we examined publication bias graphically,

using a funnel plot. All analyses were performed using STATA 14.0 and the *robumeta* macro [24].

Results

The study flowchart (**Figure 1**) shows our search strategy which resulted in the identification of 41 original research reports to be analysed.

The 41 studies analysed were all published in English: 33 were conducted in the United States[25-57], 3 in Australia[58-60], 2 in the United Kingdom[61 62], 1 in the Netherlands[63], 1 in the Czech Republic[64], and 1 internationally[65]. Thirteen studies evaluated the consequences of cannabis decriminalisation[25-28 37 58-65], 20 the consequences of legalisation of use for medical purposes[29-36 38-45 49 53-55], and 8 the consequences of legalisation of use and possession for recreational purposes[46-48 50-52 56 57]. All studies examining the effects of cannabis legalisation (for medical or recreational purposes) were based in the United States.

The reports included were heterogeneous in terms of the populations studied: 21 focused on adolescents (12-17 years)[25 28 31 33-35 38 41-44 46-50 53 55 56 61 65], 6 on young adults (18-25 years)[37 40 52 57 58 60] and 14 included data on both of these groups[14 26 27 29 30 32 36 39 45 51 58 61-63].

Among studies conducted in the United States, 9 were based on the National Study on Drug Use and Health conducted by the Substance Abuse and Mental Health Services Administration (NSDUH https://nsduhweb.rti.org/respweb/homepage.cfm)[14 31 32 36 39 42-45], 7 on the Monitoring The Future study (MTFS http://monitoringthefuture.org/)[25 28 37 38 41 50 54], 4 on the Youth Behavioral Risk Surveillance survey (YBRS https://www.cdc.gov/healthyyouth/data/yrbs/index.htm)[33-35 49] and 4 on the National Longitudinal Study of Youth (NLSY79 https://www.nlsinfo.org/content/cohorts/nlsy79[26 27], and NLSY97 https://www.nlsinfo.org/content/cohorts/nlsy97[33 40].

Among studies conducted in Australia, 2 were based on the National Drug Strategy Household Survey (NDSHS http://data.gov.au/dataset/national-drugs-strategy-household-survey).

Thirty four studies were based on repeated cross-sectional data[25 28 29 31-39 41-45 48-60 62-64], 6 on longitudinal cohort data[26 27 40 46 47 61] and one on analyses of routine administrative data[30]. Sample sizes in individual studies ranged from n=336[30] to > 11,703,100[35].

Overall, 16 studies were characterised by a very low risk of bias[14 31 32 34-36 38 41 44 45 49 50 54 58 59 63] and 9 by a low risk of bias[26 27 30 47 48 51-53 55]; in our systematic review only the results of these investigations were analysed. Given the small number of articles in each category, all studies except those with a high level of bias were meta-analysed. In additional analyses, we verified that findings were stable when studies characterised by probable bias were excluded.

Decriminalisation of cannabis use

As shown in **Table 1**, mong the 13 studies examining the consequences of cannabis decriminalisation, three were characterised by a very low risk of bias[58 59 63]. Two of these - one based in Australia (n=15,468) and the second in the Czech Republic (n=1524), and both conducted among adolescents and young adults, found no evidence of statistically significant changes in patterns of cannabis use following policy change[58 63]. However, one study - based in Australia and conducted exclusively among adolescents aged 12-17 years (n=39,0387) - observed a 12% increase in use following cannabis decriminalisation[59]. We also identified one study characterised by a low risk of bias[26] - conducted in the United States and focusing on 14-21 year olds (n=12,686) - which observed no statistically significant effect of cannabis decriminalisation on youths' use.

Meta-analysing all 13 studies, we observed an I^2 of 99.5%, indicating high heterogeneity. After excluding studies conducted by Williams & Bretteville-Jensen[59] and Miech et al.[37] (Supplementary Figures 1A & 1B), which appeared to be outliers, the I^2 was reduced to 99.1%, but remained too high to conduct a robust meta-analysis. This was unchanged when the analysis was restricted to cohort study data, study year (< or >= 2000), a particular age group (12-17 or 18-25 years), or recent cannabis use (30 days).

Legalisation of cannabis use for medical purposes

As shown in **Table 2**, twenty studies examined the consequences of the legalisation of cannabis use for medical purposes in the United States from 1996 onwards. Twelve were characterised by a very low risk of bias[31 32 34-36 38 41 44 45 49 54]. Of those, six were based on NSDUH data[14 31 32 36 44 45], three on the YRBS[34 35 49] and three on the MTFS[38 41 54]. Altogether six studies (n ranging from 11,453 to 11,703,100) - all conducted among adolescents - one additionally including youths aged 18-20 years[36] and one additionally including youths aged 18-25 years[45] - found no statistically significant effect of the introduction of medical cannabis laws[34-36 38 44 45]. Three of these studies were based on NSDUH data[36 44 45] and two on the YRBS[34 35]. Importantly, both the NSDUH and the YRBS being repeated cross-sectional surveys, the analytical methods used vary across reports in terms of length of follow-up after policy change (from 1 to 9 years), statistical methods (logistic regression[45], difference-in-differences[35], fixed-effects models[36]), as well as covariates. Still, all studies characterised by a very low risk of bias are adjusted for individual demographic characteristics (age, sex, race) as well as contextual factors (at minima a state identifier and the level of cannabis use prior to policy change). In three studies conducted among adolescents, the legalisation of medical cannabis was followed by a decrease in use[32 41 49]. These three reports were based on different large datasets (NSDUH[32], MTFS[41] and YRBS[49], with ns ranging from 11,813 to

973,089). Finally, three studies (ns ranging from 11,813 to 973,089) observed an increase in levels of cannabis use among adolescents (under 18 years) living in a state which passed medical cannabis laws[14 31 54] and one of these observed a similar effect among young adults (ages 18-25 years) [14].

Two studies were characterised by a low risk of bias[30 53]. One, based on routine data (Arrestee Drug Abuse Monitoring system – ADAM, n=336), showed no statistically significant differences in the prevalence of cannabis use (as ascertained by urine tests) among persons seen in hospital emergency departments before and after medical cannabis laws[30]. The second study reported that among cannabis users recruited via social media (n=2,630), the level of cannabis vaping and eating varied with the time since legalisation of medical cannabis – the longer the time since legalisation, the higher the likelihood of use[53].

Importantly, these data indicate that the provisions of laws enabling access to cannabis for medical purposes, such as the amount of cannabis that individuals are allowed to possess and use, the existence of patient registries[49], the proportion of dispensaries per inhabitant, the authorisation of home cultivation, or concomitant laws making it legal to use cannabis for recreational purposes[53] are influential and should be systematically reported by researchers examining the effects of cannabis policies.

Meta-analysing all 20 studies, we observed an I^2 of 100%, indicating high heterogeneity. After excluding the studies conducted by Wen et al.[36] and Harper et al.[32], which appeared to be outliers (Supplementary Figures 2A & 2B), the I^2 was reduced to 98.6%, but remained too high to conduct a robust meta-analysis. This was unchanged when the analysis was restricted to cohort studies, study year (< or >= 2000), a particular age group (12-17 or 18-25 years), or recent cannabis use (30 days).

Legalisation of cannabis for recreational purposes

As shown in **Table 3**, We identified 8 studies examining the impact of recreational cannabis laws, which make it legal to use and possess small amounts of cannabis, on youths. They were all conducted in the United States, where several states have introduced this form of cannabis legalisation since 2012. Four studies were based in Washington state[46 47 48 52], two in Colorado[56 65], one in Washington state and Colorado[50] and one in Oregon[51]. Only one study - based on the MTFS - was characterised by a very low risk of bias[50]. This investigation (n=253,902) reported a statistically significant increase in cannabis use among adolescents living in Washington state (3.2% increase among 8th graders and 5.0% increase among 10th graders), but not among those living in Colorado.

We also identified two studies characterised by a low risk of bias. One (n=13,335) reported a 2.0-3.5% increase in the frequency of cannabis use among college students living in Washington state[52] and the other an increase of .02% among middle and high school students living in Colorado (n=24,171)[65].

Meta-analysing all 8 studies, we observed an I^2 of 89.8%, indicating high heterogeneity (Supplementary Figures 3A & 3B). After excluding the study conducted by Cerda et al.[50], which appeared to be an outlier, the I^2 was reduced to 45.0%. This analysis yielded an average standardised mean difference of 0.03 (95% CI -0.01-0.07), suggesting a possible small increase in the use of cannabis following the legalisation of recreational cannabis.

Discussion

Main findings

Our systematic review of studies examining the impact of the liberalisation of cannabis legislation on patterns of use among adolescents and young people, identified 41 reports published prior to March 2018, 16 characterised by a very low risk of bias and 9 by a low risk of bias. With the exception of one study, high quality reports examining the impact of cannabis decriminalisation (n=4) show no statistically significant change in youths' patterns of use. Similarly, the legalisation of cannabis use for medical purposes, extensively evaluated in the United States, does not appear to have an effect: 6 studies suggest no change in cannabis use among youths, 3 studies observe a decrease, and 4 studies report an increase. However, the legalisation of cannabis for recreational purposes, examined in 6 studies with a very low or low risk of bias, may be associated with a small increase in levels of use among youths.

Overall, policies regarding cannabis use and possession seem to have little effect on actual patterns of use among young people, with the possible exception of the legalisation of recreational use. To date, evidence regarding the impact of the legalisation of recreational cannabis comes from the United States, where prevalence levels of substance use are high and laws liberalising cannabis use tend to be market-oriented. Additional data from other settings (e.g. Uruguay, Canada) will help gain a better understanding of relations between cannabis policy and patterns of use in the population.

Limitations and strengths

Our systematic review and meta-analysis has limitations which need to be acknowledged. First, the specific provisions of laws and policies regulating cannabis and which can influence actual access to the substance[2], vary across settings. For example, decriminalisation can imply different limits on the amount of cannabis that leads to a fine – e.g. the possession of 15 g of herb or 5 g of resin in the Czech Republic is fined approximately

550 euros[63]; in the Australian Capital Territory (Canberra region) the possession of up to 25 g is fined approximately 100 euros, while in Western Australia (Perth region) the possession of less than 10 g is tolerated but higher quantities can result in a conviction[66]. Similarly, laws allowing the use and possession of cannabis for medical purposes, currently in place in approximately 20 countries (e.g. Australia, Belgium, Spain, Canada and some U.S. states) take different forms. For instance, only the Netherlands and some U.S. states make it possible for individuals to purchase or grow cannabis that can be smoked – in other settings individuals can purchase specific medicines derived from cannabinoids (e.g. the United Kingdom). The legal age at which individuals are authorised to possess cannabis (18 or 21 years) varies across settings, with possibly differential effects on levels of use among young adults. Finally, the price of cannabis, which influences levels of use among young people[58 67], varies from place to place and over time. Clearly, differences in specific policy provisions, which have an impact on cannabis availability, make it difficult to compare different settings. Nevertheless, at the time of its implementation or even before if there is wide media coverage, policy change in and of itself can influence the perceptions of cannabis, which in turn shape levels of use[41], justifying the conduct of this systematic review. Second, the duration of follow-up varies across studies, in part because changes in cannabis policy occurred in different periods and places. This is especially a concern for reports evaluating the impact of recreational cannabis laws: policy changes introduced decades ago (e.g. the Netherlands) were not fully evaluated, while follow-up is limited for more recent policy modifications (e.g. the United States, Uruguay). It is unclear whether the introduction of policies that liberalise cannabis use and possession is most likely to influence patterns of use in the short or in the long-term; in the present report we considered that a follow-up period of at least one year following actual policy implementation was necessary to test a possible

effect. Third, among studies examining the consequences of the legalisation of cannabis for recreational purposes, we only identified one study characterised by a very low risk of bias and 5 by a low risk of bias, and the findings we report will need to be confirmed. Our attempt to meta-analyse the results of different studies included in this review proved inconclusive, with the exception of legalisation of cannabis for recreational purposes: this calls for additional, methodologically robust, studies in this area. Fourth, although changes in cannabis policies have occurred in various settings, most studies included in this report were conducted in the United States, where most research in this area has been conducted. It is difficult to assess the extent to which the findings observed in the U.S. will generalise to other countries, and it will be important to update knowledge in this area once data from other places (e.g. Uruguay, Canada) become available.

Despite these limitations, our study has several strengths: a) the evaluation of studies published in different disciplines (public health, epidemiology, economics, social policy) through multiple databases; b) the combination of data from different settings (United States, Australia, Europe); c) special attention to the risk of bias, examined using a framework especially developed for observational studies. Moreover, our systematic review takes into consideration different forms of liberalisation of cannabis policies (decriminalisation, legalisation for medical purposes and for recreational purposes), attempting to tackle this complex issue in a thorough way.

Methodological issues

The studies included in this systematic review relied on several different datasets and applied quite varied methods (logistic regression[45], difference-in-differences[35], fixed-effects models[36]), to isolate the effects of policy change on patterns of cannabis use independently

of individual and contextual characteristics; such triangulation of different methods is considered especially reliable when, as in this case, it yields consistent results[68]. Importantly, because cannabis policy changes most often occur in settings where public support and levels of use are high, it is essential to take into account levels of cannabis use prior to policy change, as was the case in all reports we considered to present a very low or low risk of bias. Finally, it is important to note that we evaluated relative changes in cannabis use post vs. pre policy change. Levels of cannabis use vary widely across settings and in some places may have been so high prior to policy change that additional increases are unlikely (this may be the case of Colorado where over 25% of 12th graders use cannabis on a monthly basis)[50].

Most studies included in our systematic review were cross-sectional, because reports based on longitudinal data are less numerous and were not always of sufficiently high quality. While repeated cross-sectional studies are well-suited to examine long-term changes in patterns of cannabis use in relation to changes in the legal context, additional evidence from longitudinal data following young people would make it possible to take into account individual characteristics and further strengthen the inference that can be drawn regarding the impact of cannabis policy change.

Implications

Summarising the available evidence, we found that, contrary to what has been observed in adults[36 58 69], cannabis decriminalisation and legalisation for medical purposes are probably not related to significant changes in patterns of use among adolescents and young people. This was also recently reported by a systematic review and meta-analysis which focused on medical cannabis laws and patterns of use in the preceding 30 days among adolescents[70]. On the other hand, the legalisation of cannabis use for recreational purposes may lead to higher levels of use in this age group and a younger age at initiation. Several hypotheses have been

proposed to explain this multifactorial phenomenon: a) changes in the reporting of cannabis use; b) a decrease in perceived harmfulness[41]; c) an increase in cannabis availability and access; d) a decrease in price (in legal outlets or on the black market)[71]. While the liberalisation of cannabis policy can have both collective and individual benefits (e.g. decrease in costs of law enforcement, increase in quality control, reduction in individuals' difficulties with the legal system), these data suggest the possibility of small negative public health implications. Adolescents and young adults are especially vulnerable to the consequences of cannabis use, in terms of both biological and social development[72 73], therefore policies that involve the legalisation of recreational use of cannabis need to be accompanied by prevention efforts targeted towards young people. The most effective prevention programs aim to improve school climate and strengthen youths' psychosocial skills such as self-esteem and conflict resolution[74 75].

Conclusion

In recent decades, cannabis policies have been liberalised in different ways (decriminalisation, legalisation of use for medical or recreational purposes) and in various settings. Our systematic review and meta-analysis of 41 research articles published across disciplines (epidemiology, economics, social policy) and using a variety of datasets and statistical methods shows that cannabis decriminalisation or legalisation of use for medical purposes do not result in higher levels of use among youths. Legalisation of use for recreational purposes appears to possibly result in a small increase. It will be important to reassess whether this tendency persists over time, varies across subgroups of youths (male vs. female, urban vs. rural, socioeconomically disadvantaged vs. favoured), and is comparable across settings, particularly as additional countries introduce changes in cannabis policy (e.g. Canada). Repeated cross-sectional as well as longitudinal studies will be

necessary to thoroughly evaluate adolescents' levels of cannabis use following changes in policy.

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Table 1. Studies examining cannabis use levels in adolescents before and after decriminalisation of cannabis possession (1981-2017).									
	Study	**Place of study**	**Type of policy change/study period**	**Participant characteristics / n**	**Study design**	**Cannabis use measures (frequency/ period)**	**Statistical methods/ covariates**	**Key findings/effect size**	**Risk of bias**
1	Johnston et al., 1981[25]	California, Maine, Minnesota, Ohio (early change) + North Carolina, New York, Missouri (late change) vs. states with no decriminalisation	Decriminalisation of cannabis possession in 1975 and 1976	12th grade students participating in the Monitoring the Future surveys (MTFS)/ n~99,000 per year	Cross-sectional survey (1975-1980)	12 months, 30 day, and daily use	Comparisons of prevalence rates	12-month use: d=0.06, 95% CI 0.0003; 0.127; 30-day use: d=0.125, 95% CI 0.059; 0.191(unadjusted)	Possible
2	Thies & Register, 1993[26]	Alaska, California, Colorado, Maine, Minnesota, Missouri, Nebraska, New York, North Carolina, Ohio, Oregon	Decriminalisation of cannabis possession 1976-1979	14-21 year olds participating in the National Longitudinal Survey of Youths1979 (NLSY) /n=12,686	Cohort study with follow-up in 1984 and 1988.	30 day use	OLS regression models controlled for sex, race, parental education, own education, income, church attendance, marital status, urban setting; legal context regarding underage drinking	1984: d=0.05, 95% CI -0.02; 0.14; 1988: d=0.06, 95% CI -0.03; 0.16 (unadjusted)	Low
3	McGeorge & Aitken, 1997[58]	Australian Capital Territory vs. Melbourne	Decriminalisation of cannabis possession, use and cultivation in 1992	3rd year university students at Australian National University and Melbourne University /n=903	Cross-sectional survey (1994)	12-month use	Chi-square statistics	d=0.21, 95% -0.02; 0.45 (unadjusted)	Probable
4	MacCoun, 1997[63]	Netherlands	Decriminalisation of cannabis in	16-18 year olds participating in a	Repeated cross-sectional	Lifetime use	Comparison of prevalence rates	Netherlands vs. US: d=-0.23; 95% CI -0.26; -	Possible

			1976 followed by legalisation in 1984	school-based survey (Trimbos) vs. Youths of the same age in the US (Monitoring the Future)/ n~115,000	surveys: 1970 to 1996			0.19 (unadjusted)	
5	Pacula 1998[27]	Alaska, California, Colorado, Maine, Minnesota, Missouri, Nebraska, New York, North Carolina, Ohio, Oregon	Decriminalisation of cannabis possession 1976-1979	14-21 year olds participating in the National Longitudinal Survey of Youths1979 (NLSY)/n=8,008	Cohort study with follow-up in 1984.	30 day use	Two part model controlled for sex, age, race, number of siblings, urban setting, academic achievement, expected years of schooling, illegal activity; parents' marital status, employment status, alcohol use; legal context regarding alcohol use, crime level, beer and cigarette taxes	d=0.0179, 95% CI -0.038; 0.0008	Low
5	DiNardo & Lemieux 2001[28]	California, Colorado, Maine, Minnesota, Mississippi, Nebraska, New York, North Carolina, Ohio, Oregon	Decriminalisation of cannabis possession 1976-1979	12th grade students participating in the Monitoring the Future surveys (MTF) /n~165,000	Cross-sectional survey (1980-1989)	30 day use	Structural regression model controlled for sex, age, race, parental education, weekly hours of work, income, alcohol use, state-level unemployment and alcohol drinking age	d=-0.08, 95% CI -0.12; -0.05	Possible
7	Williams 2004[59]	Australian Capital Territory, Northern Territory vs. non decriminalising states	Decriminalisation of cannabis possession, use and cultivation between 1988 and 1998	14-25 years , Australian National Drug Strategy Household Survey (NDSHS)	Repeated cross-sectional surveys (1988, 1991, 1993, 1995, 1998)	12-month use	Ordered probit model controlled for sex, age, marital status, dependent children, ethnicity, educational level,	d=0.04, 95% CI -0.102; 0.192	Very low

				/n=15,468			employment, capital city residence, decriminalisation regime		
8	Williams & Bretteville-Jensen, 2014[60]	South Australia, Australian Capital Territory, Northern Territory, Western Australia vs. non-decriminalising states	Decriminalisation of cannabis possession, use and cultivation between 1987 and 2004.	20-40 year old lifetime users of cannabis participating in the Australian National Drug Strategy Household Survey (NDSHS) /n=39,087	Repeated cross-sectional surveys (1998, 2001, 2004, 2007, 2010)	Age at initiation	Difference-in-differences with discrete time hazard model controlled for sex, education, ethnicity, capital city residence, survey year	12-17 years: d=0.57, 95% CI 0.52; 0.63	Very low
9	Fuller, 2014[61]	England	Declassification of cannabis from schedule B to schedule C drug (2004) and then back (2009)	11-15 year olds participating in a representative school survey/n=6,173	Repeated cross-sectional surveys (2001-2014)	12-month use	Prevalence rates	2004 vs. 2009: d=-0.22, 95% CI -0.29; -0.165 (unadjusted)	Probable
10	Braakmann & Jones, 2014[62]	United Kingdom	Declassification of cannabis from schedule B to schedule C drug (2004)	15-25 year olds participating in the Offending, Crime and Justice Survey (OCJS)/n=2,539	Cohort study (2003-2006)	12-month and 30-day use;	Difference-in-differences model controlled for age and calendar year	12-month use; 15-17 yrs: d=-0.01, 95% CI -0.07; 0.002; 18-25 yrs: d=-0.05, 95% CI -0.15; 0.05; 30-day use: 15-17 years: -0.006, 95% CI -0.009; 0.08; 18-20 years: -0.13, 95% CI -0.24; -0.02	Possible
11	Miech et al, 2015[37]	California vs. other US states	Decriminalisation in 2010	8th, 10th and 12th grade students participating in the Monitoring the Future surveys (MTF)/n=97,238	Repeated cross-sectional surveys (2007-2012)	12-month and 30-day use	GEE regression models	12-month: d=0.32, 95% CI 0.31-0.34; 30-day use: d=0.57, 95% CI 0.55-0.59 (unadjusted)	Possible
12	Shi et al, 2015[65]	Cross-national study of 38 countries	Depenalisation, decriminalisation, and partial	15 year olds participating in the Health	Repeated cross-sectional surveys	12-month and regular (>=40 times in	Multilevel logistic random intercept regression	12-month use: d=-0.004, 95% CI -0.02; 0.13; regular use:	Possible

			prohibition changed since 0-5 years, 5-10 years or >10 years	Behaviour in School-Aged Children Study (HBSC)/ n=172,894	(2001/2002, 2005/2006, 2009/2010)	lifetime) use		d=0.17, 95% CI 0.13; 0.20	
13	Červený J et al, 2017[64]	The Czech Republic	Decriminalisation of cannabis possession in 2010	15-25 years participating in drug use monitoring surveys/ n=1086 in 2008 and 438 in 2012	Repeated cross-sectional surveys (2008-2012)	Age at initiation	Mixed proportional hazards controlled for sex, education, birth cohort and region of residence	d=-0.26, 95% CI -0.37; -0.15 (unadjusted)	Very low

Table 2. Studies examining cannabis use levels in adolescents before and after the legalisation of cannabis use for medical purposes (1996-2018).

	Study	Place of study	Type of policy change/study period	Participant characteristics / n	Study design	Cannabis use measure (frequency/ period)	Statistical methods/ covariates	Key findings/effect size	Risk of bias
1	Khatapoush & Hallfors, 2004[29]	California (CA)	State-level Medical marijuana laws (MML): Proposition 215 (1996)	16-25 year olds participating in the Robert Wood Johnson Foundation's Fighting Back initiative (FB)/n=2,651	Repeated cross-sectional surveys in 1995, 1997 and 1999.	12-month and 30-day use	Logistic regression model	12-month use: d=0.54, 95% CI 0.48; 0.59; 30-month use: d=0.72, 95% CI 0.64; 0.79 (unadjusted)	Probable
2	Gorman et al, 2007[30]	Los Angeles, San Diego, San Jose (CA), Portland (OR)	State-level Medical marijuana laws (MML) introduced before 2002	10-18 year olds registered in the Arrestee Drug Abuse Monitoring system (ADAM)/ on average n=255 in California & n=81 in Oregon	Routine data collection (1995-2002)	Urine test data (>=50 ng of THC per decilitre)	Interrupted time series design	California: 10-18 yrs: d=-0.42, 95% CI -0.60; -0.24; Oregon: 10-18 yrs: d=-0.75, 95% CI -1.33; -0.17 (unadjusted)	Low
3	Wall et al, 2011[31]	Alaska, California, Colorado, Hawaii, Maine, Nevada, Oregon, Washington + Michigan, Montana, New Mexico, Rhode Island, Vermont + Arizona, Delaware, New Jersey vs. other US states	State-level Medical marijuana laws (MML) introduced before 2002	12-17 olds participating in the National Survey of Drug Use and Health (NSDUH)/ n~11,813	Repeated cross-sectional surveys (2002-2008)	30-day use	Fixed effects model with random intercept, controlled for cannabis use 2002-2008	2002-2003: d=0.15, 95% CI 0.07; 0.23	Very low

4	Harper et al, 2012[32]	Alaska, California, Colorado, Hawaii, Maine, Nevada, Oregon, Washington + Michigan, Montana, New Mexico, Rhode Island, Vermont vs. other US states	State-level Medical marijuana laws (MML) introduced before 2002	12-17 year olds and 18-25 year olds participating in the National Survey of Drug Use and Health (NSDUH) /n~11,813 per age group	Repeated cross-sectional surveys (2002-2009)	30-day use	Difference-in-differences estimates controlled for measurement error	12-17 years: d=-1.25, 95% CI –1.29; -1.21; 18-25 years: d=1.71, 95% CI 1.67 - 1.75	Very low
5	Anderson et al, 2012[33]	Alaska, Arizona, California, Colorado, Delaware, District of Columbia, Hawaii, Maine, Michigan, Montana, Nevada, New Jersey, New Mexico, Oregon, Rhode Island, Vermont, Washington vs. other US states	State-level Medical marijuana laws (MML) introduced before 2011	15-19 years olds participating in the National and State Youth Risk Behavior Surveys (YRBS) /n=786,568	Repeated cross-sectional surveys (1993-2011)	30-day use; 30-day frequent use;	Linear regression controlled for age, sex, race, grade, state-level marijuana decriminalisation, BAC 0.08 laws, state beer tax, income per capita, unemployment	YRBS: 30day use: d=-0.32, 95% CI -0.33; -0.32; 30-day frequent use d=-0.18, 95% CI -0.19; -0.18	Possible
6	Lynne-Landsman et al, 2013[34]	Delaware, Michigan, Montana, Rhode Island compared pre and post-MML implementation	State-level Medical marijuana laws (MML) introduced 2003-2009	9-12th graders participating in the Youth Risk Behavior Surveys (YRBS) /n~11,453	Repeated cross-sectional surveys (2003-2009)	30-day use;	Difference in differences controlled for age, ethnicity, and sex	d=0.24, 95% CI 0.20;0.28	Very low
7	Choo et al, 2014[35]	Idaho vs. Montana, Massachusetts vs. Rhode Island, New Hampshire vs. Maine, Utah vs. Nevada, New York vs. Vermont	State-level Medical marijuana laws (MML)	9-12th graders participating in the Youth Risk Behavior Surveys (YRBS)/ n~11,703,100	Repeated cross-sectional surveys since 1991, 1993, 1995, 1997, 1999, 2001, 2003, 2005, 2007	30 day use	Difference-in-differences controlled for state, year, age, sex, race, grade	d=0.065, 95% CI 0.026; 0.105	Very low
8	Wen et al, 2014[36]	District of Columbia,	State-level Medical	12-20 year olds participating in	Repeated cross-sectional	30-day use;	Fixed-effects models controlled	d=-1.72, 95% CI:-1.73;-1.71	Very low

		Michigan, Montana, New Jersey, New Mexico, Rhode Island, Vermont vs US states with no MML laws by 2010	marijuana laws (MML) introduced between 2004 and 2010	the National Survey on Drug Use and Health (NSDUH)/ n~183,600	surveys (2004-2011)		for age, sex, race, self-reported health, cigarette use, urban residence, family poverty, state-level unemployment, mean income, median income, alcohol excise taxes.		
9	Hasin et al, 2015[38]	21 US states that passed MML vs. non-MML US states	State-level Medical marijuana laws (MML) introduced by 2014	8th, 10th and 12th grade (13, 15, 17) students participating in the Monitoring the Future surveys (MTF) /n=1,098,070	Repeated cross-sectional surveys (1991-2014)	30-day use;	Multilevel regression models controlled for sex, age, race, parental education, class size, private school, urban setting, state-level proportion of males, whites, persons with no high school education and aged 11-24 years	d=-0.033, 95% CI -0.039; -0.026	Very low
10	Schuermeyer et al, 2015[39]	Colorado vs. 34 non-MML US states	State-level Medical marijuana laws (MML) introduced in 2009	12-20 year olds participating in the National Survey on Drug Use and Health (NSDUH)/ n~158,600 12-17 year olds + 159,200 18-25 year olds	Repeated cross-sectional surveys (2006-2011)	>=20 times in 30-days use	Logistic regression controlled for state, year, age, sex, race, educational level and state-by-year interaction	12-17 yrs: d=0.09, 95% CI -0.04 ; 0.23; 18-25 yrs: 0.23, 95% CI 0.16-0.29 (unadjusted)	Possible
11	Pacula et al, 2015[40]	Alaska, Arizona, California, Colorado, Delaware, District of Columbia,	State-level Medical marijuana laws (MML) introduced before	- <21 year olds participating in the National Longitudinal Survey of	Cohort study (1997-2011)	30-day use;	Difference-in-differences models controlled for population unemployment	d=-0.0109, 95% CI, -0.03; 0.009	Possible

		Hawaii, Maine, Maryland, Michigan, Montana, Nevada, New Jersey, New Mexico, Oregon, Rhode Island, Vermont, Washington vs. US states with no MML in 2012	2012; comparison of different legal provisions: patient registry; home cultivation; legal dispensaries;	Youths1997 (NLSY)/46,375			rate, age distribution, state beer tax rate, BAC 0.08 tax;		
12	Keyes et al, 2016[41]	21 US states that passed MML vs. non-MML US states	State-level Medical marijuana laws (MML) introduced by 2014	8th, 10th and 12th grade (13, 15, 17) students participating in the Monitoring the Future surveys (MTF) /n=973,089	Repeated cross-sectional surveys (1991-2014)	30-day use;	Time-varying multilevel regression models controlled for sex, age, race, parental education, class size, private school, urban setting, state-level proportion of males, whites, persons with no high school education and aged 11-24 years	d=-0.03, 95% CI -0.03;-0.027	Very low
13	Maxwell & Mendelson, 2016[42]	California, Colorado and Washington vs. other US States	State-level Medical marijuana laws (MML) and Recreational marijuana laws (RML)	12-25 year olds participating in the National Survey of Drug Use and Health (NSDUH)	Repeated cross-sectional surveys (2002-2013)	12-month use	Comparison of prevalence rates	Impossible to calculate	Probable
14	Stolzenberg et al, 2016[43]	Alaska, Arizona, California, Colorado, Delaware, Hawaii, Maine, Michigan, Montana, Nevada,	State-level Medical marijuana laws (MML) introduced between 1998 and 2011	12-17 olds participating in the National Survey of Drug Use and Health (NSDUH) /n~112,500	Repeated cross-sectional surveys (2002-2011)	30-day use	Random effects model controlled for state-level medical cannabis possession limit, cannabis availability, %	d=0.060, 95% CI 0.034;0.087	Possible

		New Jersey, New Mexico, Oregon, Rhode Island, Vermont, Washington vs. other US states					enrolled in drug class, alcohol use, prior crime conviction, % families on income assistance, % juveniles who skipped school, % families where the father resides in household, % male, % white		
15	Wall et al, 2016[44]	Arizona, Delaware, Michigan, Montana, New Jersey, New Mexico, Rhode Island, Vermont vs. other US states	State-level Medical marijuana laws (MML) introduced between 2004 and 2011	12-17 olds participating in the National Survey of Drug Use and Health (NSDUH) /n~112,500	Repeated cross-sectional surveys (2002-2011)	30-day use	Fixed effects model	d=-0.0059, 95% CI -0.030;0.018	Very low
16	Martins SS et al, 2016[45]	Arizona, Connecticut, Delaware, Illinois, Massachusetts, Michigan, New Hampshire, New Jersey, New Mexico, Rhode Island vs. other US states	State-level Medical marijuana laws (MML) introduced between 2005 and 2013	12-17 and 18-25 year olds participating in the National Survey of Drug Use and Health (NSDUH)/ n=175,000 12-17 year olds and 175,000 18-25 year-olds	Repeated cross-sectional surveys (2004-2013)	30-day use	Multilevel logistic regression controlled for sex, ethnicity, insurance status, household income, population density, state proportions of sex, ethnicity, youths, education, unemployment, median household income	12-17 yrs: d=0.02, 95% CI -0.04-0.08; 18-25 yrs: d=0.006, 95% CI -0.035 ; 0.047).	Very low
17	Johnson et al, 2017[49]	Alaska, Arizona, Colorado, Delaware, Maine, Michigan, Montana, Nevada, New Jersey, New Mexico, Rhode Island, Vermont vs.	State-level Medical marijuana laws (MML) introduced between 1998 and 2011	9-12th graders (14-17) participating in the Youth Risk Behavior Surveys (YRBS) /n=715,014	Repeated cross-sectional surveys (1991-2011)	30-day use and 30-day heavy use (>=20 times)	Fixed effect multiple logistic regression controlled for year, state, age, sex, ethnicity	30-day use: d=-0.042, 95% CI -0.051;-0.032; 30-day heavy use: d=0.0001, 95% CI -0.018;0.0185	Very low

		other US states							
18	Borodovsky et al, 2017[53]	Alaska, Colorado, District of Columbia, Oregon, Washington vs. 20 US states that did not	Legalisation status: MML or RCCL vs. no legal cannabis law	14-18 year olds recruited online (via targeted Facebook invitations) /n=2,630	Cross-sectional survey (April 29-May 18, 2016)	30-day cannabis use via smoking, vaporizing, or eating.	Logistic and linear regression controlled for age, gender, race, grade level, lifetime days of cannabis use, age of onset.	d=0.064, 95% CI -0.048;0.176	Low
19	Mauro et al, 2017[14]	Arizona, Connecticut, Delaware, Illinois, Maine, Michigan, New Hampshire, New Jersey, New Mexico, Rhode Island, vs. 27 US states with no MML by 2013	State-level Medical marijuana laws (MML) introduced prior to 2015	12-17 and 18-25 year olds participating in the National Survey of Drug Use and Health (NSDUH) /n~175,000 12-17 year-olds and 175,000 18-25 year year olds	Repeated cross-sectional surveys (2004-2013)	State-level 30-day and daily use	Multilevel linear regression controlled for trends in marijuana use and state-level % males, % White, % aged 10-24 years, % > 25 yrs with no high school degree, % unemployed, median household income.	30-day use: 12-17 years: d=0.041, 95% CI 0.022; 0.059; 18-25 years: d=0.016, 95% CI 0.003; 0.029; daily use: 12-17 years: d=-0.003, 95% CI -0.021; 0.014; 18-25 years: d=0.064, 95% CI 0.050; 0.078	Very low
20	Cerda et al, 2018[10]	Arizona, California, Colorado, Connecticut, Delaware, Illinois, Maine, Maryland, Massachusetts, Michigan, Minnesota, Montana, Nevada, New Hampshire, New Jersey, New Mexico, New York, Oregon, Rhode Island, Vermont, Washington vs. other US states	State-level Medical marijuana laws (MML) introduced prior to 2015; time since legalisation.	8th, 10th and 12th graders (13, 15, 17) participating in the Monitoring the Future Survey/ n=1,140,768	Repeated cross-sectional survey (1991-2015)	30-day use	Difference-in-differences models controlled for individual grade, age, sex, race/ethnicity, socioeconomic status, number of students per grade, public vs. private school, school in metropolitan statistical area, state-level % males, % White, % aged 10-24 years, and % older than 25 with no high school degree.	d=0.0176, 95% CI 0.0170;0.0182	Very low

Table 3. Studies examining cannabis use levels in adolescents before and after legalisation of recreational cannabis use (2016-2018).

	Study	Place of study	Type of policy change/study period	Participant characteristics / n	Study design	Cannabis use measure (frequency/ period)	Statistical methods/ covariates	Key findings	Risk of bias
1	Estoup et al, 2016[46]	Washington	Legalisation in 2012	High school students (14-17) with problematic substance use enrolled in high school in the Seattle area/ n=262	Cohort study (2010-2015)	3-month use	Mediation model	d=0.061, 95% CI -0.110; 0.232 (unadjusted)	Possible
2	Mason et al, 2016[47]	Washington vs. other US states	Legalisation in 2012	8th graders (14) in Tacoma, WA participating in a longitudinal study/n=238	Cohort study (2010/2011-2012/2013)	30-day use	Multilevel regression models controlled for substance use initiation prior to baseline	d=0.323, 95% CI -0.177; 0.825	Low
3	Fleming et al, 2016[48]	Washington vs. other US states	Legalisation in 2012	10th (16) graders participating in the biennial Washington state school survey/n=30,365	Repeated cross-sectional surveys (2000-2014)	30-day use	Logistic regression analyses controlled for perceived harm of marijuana, alcohol use, and year	d=0.044, 95% CI -0.019; 0.069	Low
4	Cerdá et al, 2017[50]	Colorado and Washington vs. other US states	Legalisation in 2012	13-18 years participating in the Monitoring the Future surveys (MTF)/ n= 253,902	Repeated cross-sectional surveys (2010-2015)	30-day use	Difference-in-differences	d=1.03, 95% CI 1.00; 1.06	Very low
5	Kerr et al, 2017[51]	2 universities in Oregon vs. 6 in	Legalisation in 2015	18-26 year old college	Repeated cross-sectional	30-day use	Mixed-effects logistic regression	d=0.0139, 95% CI 0.048; 0.075	Low

		other US states		undergraduates participating in the Healthy Minds Study/n=10,924	surveys (2014 and 2016)		controlled for cigarette use, year in college, age, sex, race, residential type, relationship status, sexual orientation, international student status, depression, anxiety, adjustment, institution size and survey period		
6	Miller et al, 2017[52]	Washington	Legalisation in 2012; Opening of licensed retail stores for marijuana in 2014	College students participating in the National College Health Assessment (WSU NCHA)/n=13,335	Repeated cross-sectional surveys (2005, 2006, 2008, 2010, 2012, 2014, 2015)	30-day use	Logistic regression controlled for age, sex, race, year in school, estimated secular increase in cannabis use.	Post MML (2014): d=0.04, 95% CI 0.002 ; 0.083; post-RML (2015): d=0.082, 95% CI 0.034 ; 0.130	Low
7	Harpin et al, 2018[66]	Colorado	Legalisation in 2012	6-12th grade (11-17) students (Healthy Kids Colorado Survey)/n=24,171	Repeated cross-sectional survey (2013 and 2014)	30-day use	Comparison of prevalence rates	d=0.006, 95% CI -0.026; 0.038 (unadjusted)	Low
8	Jones et al., 2018[57]	Colorado	Legalisation in 2012	College students(22-24 years) n=1,413	Repeated cross-sectional survey (October 2013, March 2014, October 2014 and March 2015)	Lifetime	Comparison of prevalence rates	d=-0.215, 95% CI -0.385; -0.039 (unadjusted)	High

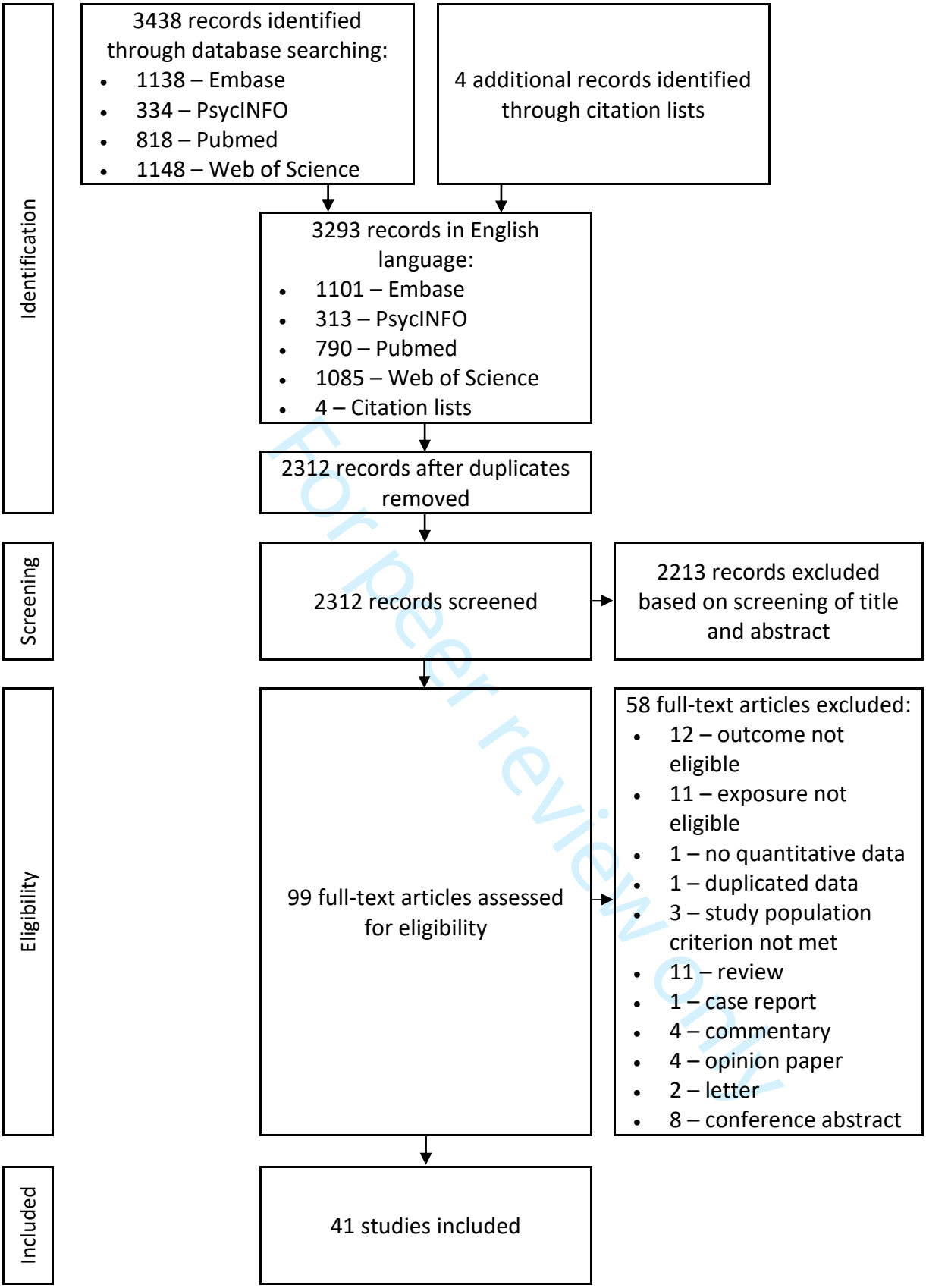


Figure 1. Flowchart showing the screening and selection process of articles selected for the study of the impact of liberalisation of cannabis policy with regard to levels of use in adolescents and young adults.

Supplementary file 1. Full search strategy

Platform: Pubmed

Notes:

1- [MH] indicates MesH Terms
2- [TW] indicates Text Word. Terms that are qualified with this field tag were searched in the following fields: title, abstract, MeSH headings and subheadings, other terms field (which includes author-supplied keywords), secondary source identifier
3- Terms qualified with * were searched with their variations (for different endings)

Search string:

(law*[MH] OR law*[TW] OR decriminalization[MH] OR decriminalization[TW] OR legalization[MH] OR legalization[TW])

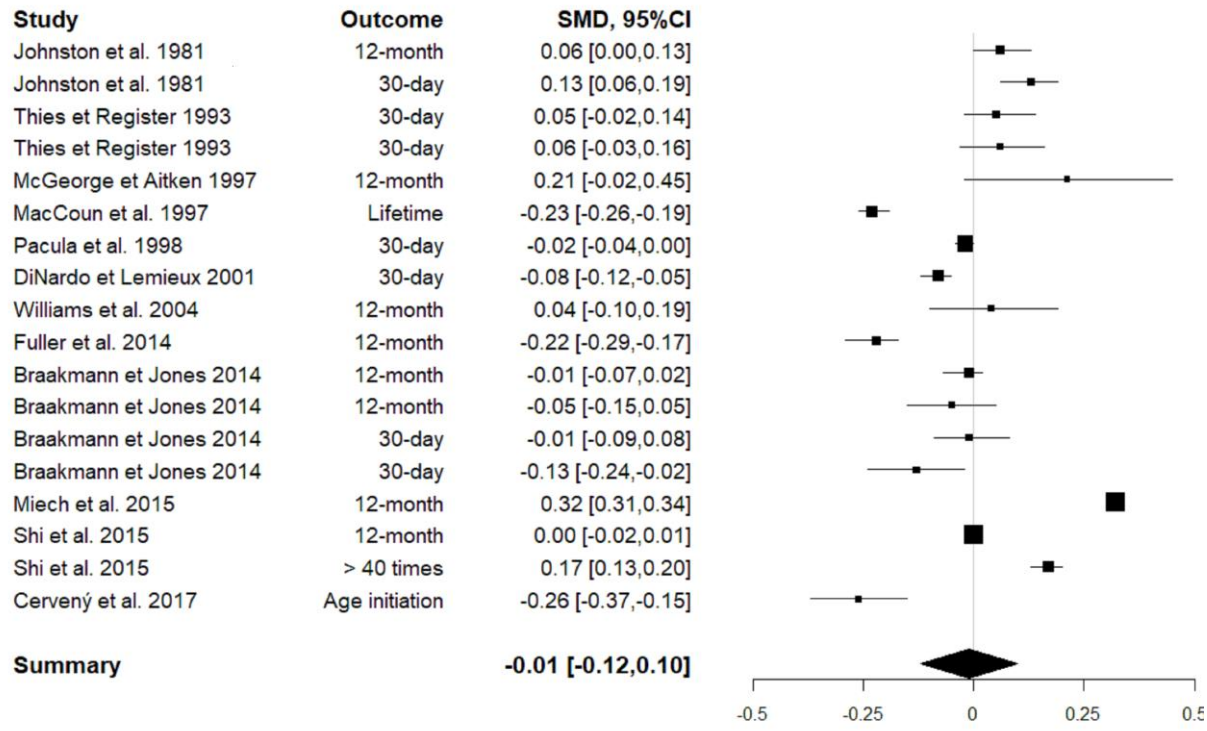
AND

(cannabis[MH] OR cannabis[TW] OR pot[MH] OR pot[TW] OR weed[MH] OR weed[TW] OR marijuana[MH] OR marijuana[TW] OR grass[MH] OR grass[TW])

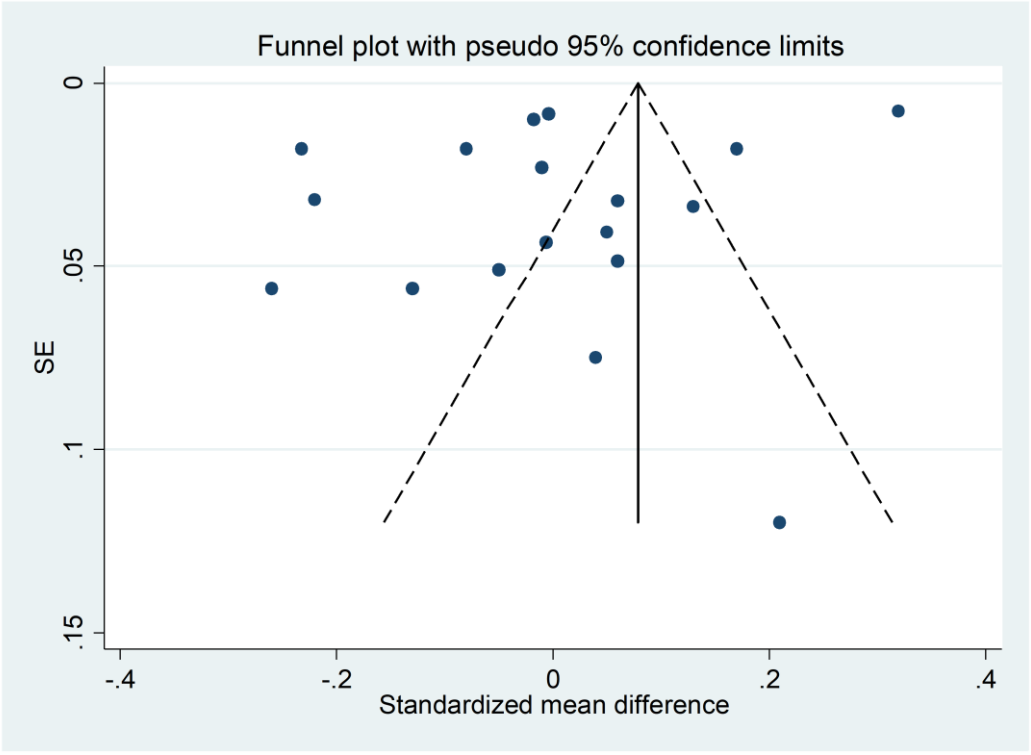
AND

(young[MH] OR young[TW] OR youth[MH] OR youth[TW] OR adolescen*[MH] OR adolescen*[TW] OR teen*[MH] OR teen*[TW] OR school*[MH] OR school*[TW] OR student[MH] OR student[TW])

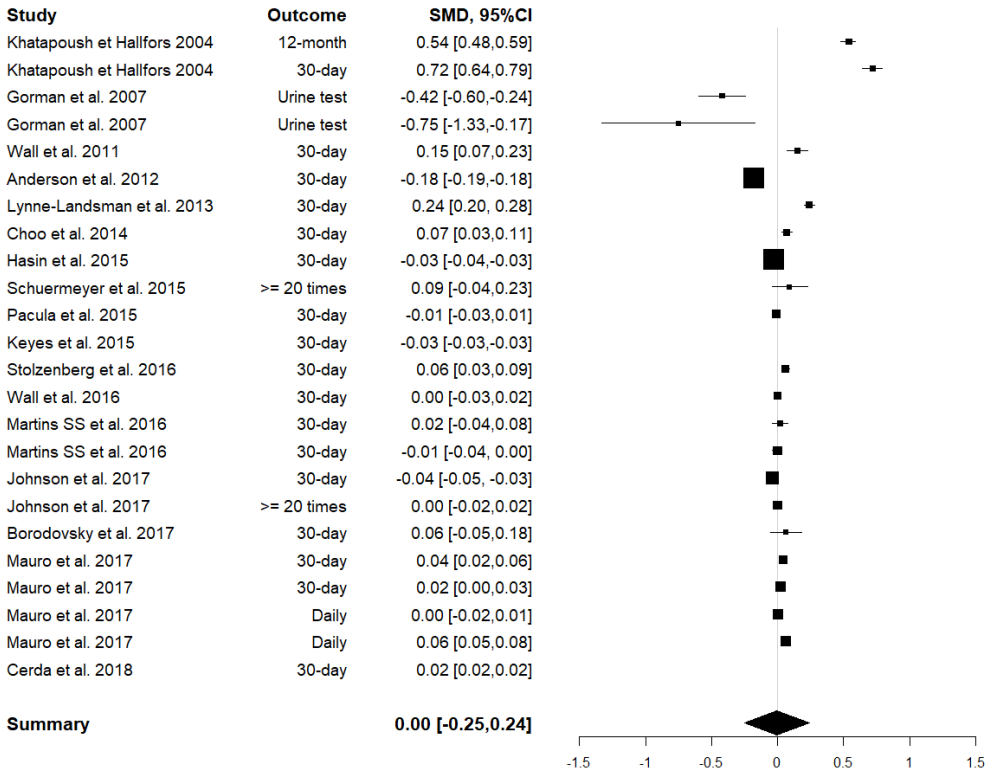
Limits: English language



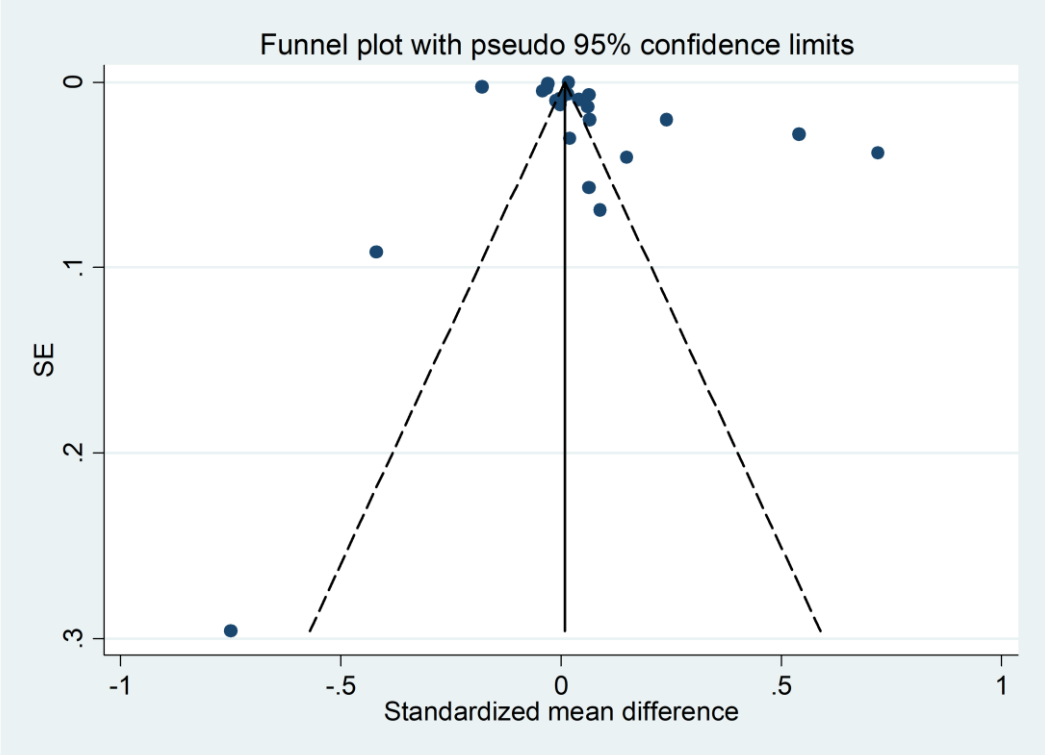
Supplementary Figure 1A: Meta-analysis of studies examining the relationship between cannabis decriminalization and levels of use in adolescents and young adults (12-25 years, prior to March 2018).



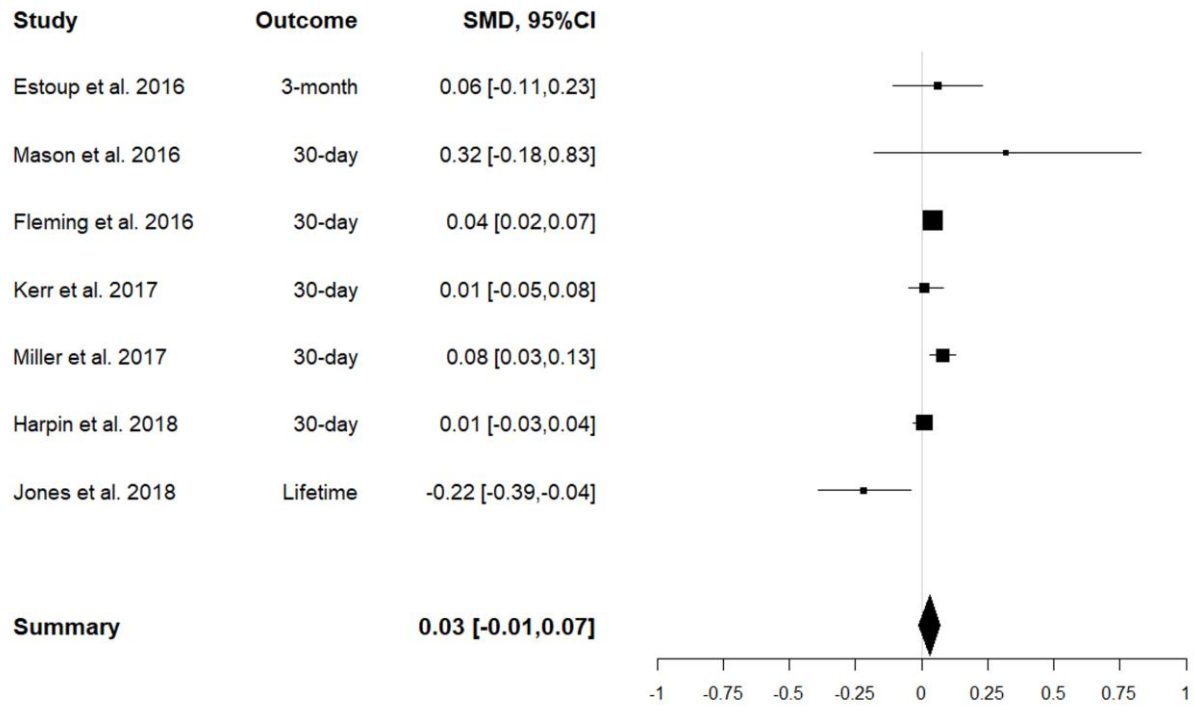
Supplementary Figure 1B: Funnel plot of studies examining the relationship between cannabis decriminalisation and levels of use in adolescents and young adults (12-25 years, I^2=99.1%, prior to March 2018).



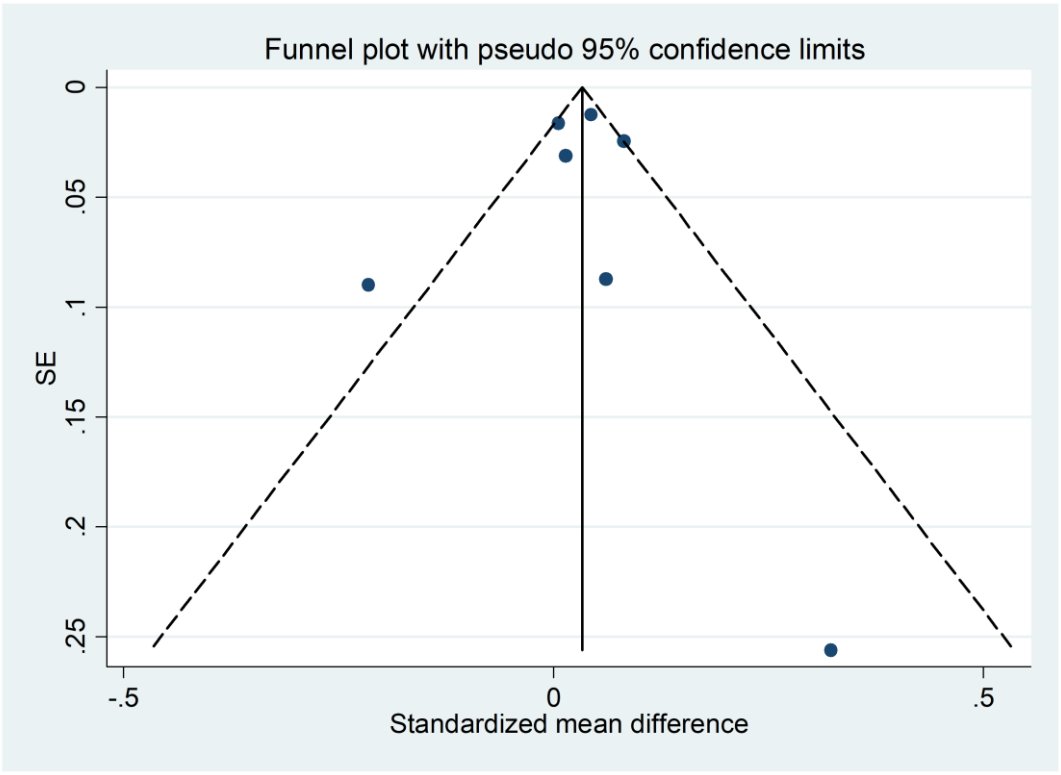
Supplementary Figure 2A: Meta-analysis of studies examining the relationship between the legalisation of cannabis for medical purposes and levels of use in adolescents and young adults (12-25 years, prior to March 2018).



Supplementary Figure 2B: Funnel plot of studies examining the relationship between legalisation of cannabis for medical purposes and levels of use in adolescents and young adults (12-25 years, I^2=98.6%, prior to March 2018).



Supplementary Figure 3A: Meta-analysis of studies examining the relationship between the legalisation of cannabis for recreational purposes and levels of use in adolescents and young adults (12-25 years, prior to March 2018).



Supplementary Figure 3B: Funnel plot of studies examining the relationship between legalisation of cannabis for recreational purposes and levels of use in adolescents and young adults (12-25 years, I^2=45.0%, prior to March 2018).

PRISMA-DTA Checklist

Section/topic	#	PRISMA-DTA Checklist Item	Reported on page #
TITLE / ABSTRACT			
Title	1	Identify the report as a systematic review (+/- meta-analysis) of diagnostic test accuracy (DTA) studies.	1 & 2
Abstract	2	Abstract: See PRISMA-DTA for abstracts.	2-3
INTRODUCTION			
Rationale	3	Describe the rationale for the review in the context of what is already known.	5-6
Clinical role of index test	D1	State the scientific and clinical background, including the intended use and clinical role of the index test, and if applicable, the rationale for minimally acceptable test accuracy (or minimum difference in accuracy for comparative design).	6
Objectives	4	Provide an explicit statement of question(s) being addressed in terms of participants, index test(s), and target condition(s).	6
METHODS			
Protocol and registration	5	Indicate if a review protocol exists, if and where it can be accessed (e.g., Web address), and, if available, provide registration information including registration number.	6-8
Eligibility criteria	6	Specify study characteristics (participants, setting, index test(s), reference standard(s), target condition(s), and study design) and report characteristics (e.g., years considered, language, publication status) used as criteria for eligibility, giving rationale.	7-8
Information sources	7	Describe all information sources (e.g., databases with dates of coverage, contact with study authors to identify additional studies) in the search and date last searched.	6-7
Search	8	Present full search strategies for all electronic databases and other sources searched, including any limits used, such that they could be repeated.	6-7
Study selection	9	State the process for selecting studies (i.e., screening, eligibility, included in systematic review, and, if applicable, included in the meta-analysis).	6-7
Data collection process	10	Describe method of data extraction from reports (e.g., piloted forms, independently, in duplicate) and any processes for obtaining and confirming data from investigators.	8
Definitions for data extraction	11	Provide definitions used in data extraction and classifications of target condition(s), index test(s), reference standard(s) and other characteristics (e.g. study design, clinical setting).	8
Risk of bias and applicability	12	Describe methods used for assessing risk of bias in individual studies and concerns regarding the applicability to the review question.	6-7
Diagnostic accuracy measures	13	State the principal diagnostic accuracy measure(s) reported (e.g. sensitivity, specificity) and state the unit of assessment (e.g. per-patient, per-lesion).	N/A
Synthesis of results	14	Describe methods of handling data, combining results of studies and describing variability between studies. This could include, but is not limited to: a) handling of multiple definitions of target condition. b) handling of multiple thresholds of test positivity, c) handling multiple index test readers, d) handling of indeterminate test results, e) grouping and comparing tests, f) handling of different reference standards	8-9

PRISMA-DTA Checklist

Section/topic	#	PRISMA-DTA Checklist Item	Reported on page #
Meta-analysis	D2	Report the statistical methods used for meta-analyses, if performed.	8-9
Additional analyses	16	Describe methods of additional analyses (e.g., sensitivity or subgroup analyses, meta-regression), if done, indicating which were pre-specified.	8-9
RESULTS			
Study selection	17	Provide numbers of studies screened, assessed for eligibility, included in the review (and included in meta-analysis, if applicable) with reasons for exclusions at each stage, ideally with a flow diagram.	9-10
Study characteristics	18	For each included study provide citations and present key characteristics including: a) participant characteristics (presentation, prior testing), b) clinical setting, c) study design, d) target condition definition, e) index test, f) reference standard, g) sample size, h) funding sources	10-11, Tables 1, 2&3
Risk of bias and applicability	19	Present evaluation of risk of bias and concerns regarding applicability for each study.	11-14
Results of individual studies	20	For each analysis in each study (e.g. unique combination of index test, reference standard, and positivity threshold) report 2x2 data (TP, FP, FN, TN) with estimates of diagnostic accuracy and confidence intervals, ideally with a forest or receiver operator characteristic (ROC) plot.	N/A
Synthesis of results	21	Describe test accuracy, including variability; if meta-analysis was done, include results and confidence intervals.	11-12; 13; 14
Additional analysis	23	Give results of additional analyses, if done (e.g., sensitivity or subgroup analyses, meta-regression; analysis of index test: failure rates, proportion of inconclusive results, adverse events).	11-12; 13; 14
DISCUSSION			
Summary of evidence	24	Summarize the main findings including the strength of evidence.	14-15
Limitations	25	Discuss limitations from included studies (e.g. risk of bias and concerns regarding applicability) and from the review process (e.g. incomplete retrieval of identified research).	15-17
Conclusions	26	Provide a general interpretation of the results in the context of other evidence. Discuss implications for future research and clinical practice (e.g. the intended use and clinical role of the index test).	18-19
FUNDING			
Funding	27	For the systematic review, describe the sources of funding and other support and the role of the funders.	N/A

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Does liberalisation of cannabis policy influence levels of use in adolescents and young adults? A systematic review and meta-analysis

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Does liberalisation of cannabis policy influence levels of use in adolescents and young adults? A systematic review and meta-analysis

Keywords : cannabis, marijuana, decriminalisation, legalisation, epidemiology, adolescents, young adults

Abstract

Objectives: To examine the effect of the introduction of policies liberalising cannabis use and possession (decriminalisation, legalisation) on adolescents' and young adults' levels of use.

Design: Systematic review and meta-analysis.

Data Sources/Search strategy: Pubmed, PsycINFO, Embase and Web of Science were searched through March 1st 2018. Original research reports were searched for terms including (law* OR decriminalisation OR legalisation) AND (cannabis OR pot OR weed OR marijuana OR grass) AND (young OR youth OR adolescen* OR teen* OR school* OR student), looked for in MeSH terms and in the text.

Data extraction and synthesis: Two independent readers reviewed the eligibility of titles and abstracts, read eligible articles, and four authors assessed the risk of bias (Quality Assessment Tool for Observational Cohort and Cross-Sectional Studies). Extracted data were meta-analysed. The protocol was registered with PROSPERO (CRD42018083950).

Results: Altogether, 3438 records were identified via search terms and 4 via citation lists; 2312 were retained after removal of duplicates, 99 were assessed for eligibility and 41 original research reports were included in our systematic review. Among them, 13 examined cannabis decriminalisation, 20 legalisation for medical purposes and 8 legalisation for recreational purposes. Findings regarding the consequences of cannabis decriminalisation or legalisation for medical purposes were too heterogeneous to be meta-analysed. Our systematic review and meta-analysis suggest a small increase in cannabis use among

adolescents and young adults following legalisation of cannabis for recreational purposes (standardised mean difference of 0.03, 95% CI -0.01-0.07). Nevertheless, studies characterised by a very low/low risk of bias showed no evidence of changes in cannabis use following policy modifications.

Conclusions: Cannabis policy liberalisation does not appear to result in significant changes in youths' use, with the possible exception of legalisation for recreational purposes which requires monitoring over time.

Strengths and limitations of this study

- To date, this is the first study to attempt to summarise research on the consequences of various types of changes in cannabis laws and policies (decriminalisation as well as different forms of legalisation) with regard to patterns of use among adolescents and young adults.
- Various data sources in the fields of public health, economics, and public policy were systematically searched in a systematic way. The risk of bias of each study was ascertained using a tool validated for observational studies.
- The duration of follow-up varied across studies, partly because changes in cannabis policy occurred in different periods and places.
- Among studies examining the consequences of the legalisation of cannabis for recreational purposes, only one was characterised by a very low risk of bias and 5 by a low risk of bias, therefore the findings will need to be confirmed in future research.

Introduction

Cannabis is one of the most frequently used psychoactive substances in North America, Europe, Oceania, and North Africa (12-month prevalence of 3.8% in the world)[1]. Since the 1961 Single Convention on Narcotic Drugs, cannabis is illegal in most countries. However, in the past 20 years a majority of US states (thirty one including the District of Columbia) and several countries (e.g. Spain, Uruguay, Portugal) have liberalised their cannabis legislation by decriminalising or legalising use for medical or recreational purposes[2]. Decriminalisation is the reduction of penalties for cannabis use, while maintaining penalties for cannabis supply. Legalisation is the permission to use and supply oneself (via home growing or controlled sale). Legalisation for medical use is permission to use and sometimes supply with the involvement of a medical professional (e.g. with a doctor's prescription or recommendation)[3].

In many settings - especially where cannabis is widely used – public support for legalisation is widespread[4 5]. For cannabis users, decriminalised or regulated access to the substance decreases the legal and criminal risks incurred. Potential collective benefits of cannabis policy liberalisation include: a) reduced law enforcement costs, b) improvements in the quality of the substance used, c) in case of commercial legalisation, additional tax revenue[6].

Still, cannabis is a source of addiction and can have deleterious health consequences in the short and long-terms, including impairments in memory and concentration[7], risk of injury, or respiratory problems[8]. Moreover, liberalised access to cannabis could also influence the levels of use of other psychoactive substances (e.g. tobacco, alcohol)[9 10]. At the same time, there is also evidence that in the United States, the recent increase in opioid use

is less marked in states which recently implemented policies liberalising cannabis regulations[11].

In adults, the liberalisation of cannabis policy has been followed by increases in levels of heavy cannabis use[12-15]. This may be driven by reductions in the perceived risks[16], price decreases, as well as increases in cannabis availability[13 15]. However, in adolescents, who may be especially vulnerable to the negative consequences of cannabis[7], the impact of policy liberalisation is unclear[13]. As additional US states and European countries are considering liberalising cannabis legislation, there is need to evaluate the potential public health consequences of such policy change.

The objectives of this study were to gain better understanding of the influence of changes in cannabis policy on patterns of use among adolescents and young adults. Youths are a high risk group in terms of illegal substance use and may be especially sensitive to changes in policy; at the same time they may also be especially vulnerable to the biological, psychological and behavioural consequences of cannabis. Data published before March 1st 2018 on this topic were systematically reviewed and meta-analysed.

Methods

Search strategy

Following PRISMA guidelines[17], we conducted a systematic review of studies testing quantitative differences in cannabis use among adolescents and young adults before and after policy change, published prior to March 1, 2018.

Specifically, the following search terms were introduced in Pubmed, Web of Science, EMBASE, PsycINFO: (law* OR decriminalisation OR legalisation) AND (cannabis OR pot OR weed OR marijuana OR grass) AND (young OR youth OR adolescen* OR teen* OR school* OR student). Searches were specified for both MeSH terms and text words and were modified to

meet the requirements of each database. Only articles in English were identified. All titles and abstracts were independently screened by two of the authors to determine potential eligibility. Full texts of all potentially eligible studies were read by two of the authors (FH, MAdS) and discussed with all other authors in case of disagreement. The protocol was registered in PROSPERO (CRD42018083950) and followed the PRISMA framework[17]. The full search strategy is detailed in Supplementary material (Figure 1).

Inclusion criteria

To be included, studies had to be conducted among individuals younger than 25 years and quantitatively assess whether cannabis policy change (defined as decriminalisation, or legalisation of cannabis use for medical or recreational purposes) as compared to no change or the situation prior to change, was associated with changes in cannabis use. This age limit was selected as it is a meaningful cut-off for the potentially negative biological and social effects of cannabis[7] as well as a frequently-used upper bound to define young people. We excluded articles: a) exclusively based on participants older than 25 years; b) only reporting changes in perceptions of cannabis use; c) not including at least two measures of cannabis use and which did not make it possible to compare changes between before and after policy change; d) not including quantitative data; e) reviews, letters, opinions and policy papers.

Patient and public involvement

This research was based on analyses of previously published studies and did not involve direct patient involvement.

Risk of bias

In order to judge the quality of studies that were analysed, risk of bias was assessed using the Quality Assessment Tool for Observational Cohort and Cross-Sectional Studies developed by the National Institute of Health (NIH) (https://www.nhlbi.nih.gov/health-

pro/guidelines/in-develop/cardiovascular-risk-reduction/tools/cohort). Four independent raters evaluated each study (two per article) on up to 11 items including characteristics of the study population, exposure and outcome measurement, time frame adequacy, loss to follow-up (cohort studies; <20% being considered as associated with low bias), adjustment for confounders. Each item received one point, and the scale was transformed to range from 0-10. Both raters' scores were summed and averaged. We considered ratings >=9.5 indicative of very low, 9-9.4 of low, 7.1-9 of possible, 5.1-7 of probable and <5 of high risk of bias. Studies defined as presenting a very low risk of bias had no identified flaws. Studies characterised by a low risk of bias provided insufficient information regarding the study time frame or loss to follow-up (where applicable). Studies considered to present a possible risk of bias were characterised by any of the following: a) insufficient information about the study population recruitment or follow-up (where applicable), b) insufficient definition of exposure or outcome, c) a study period of < 1 year between exposure and outcome, or d) insufficient adjustment for potentially confounding individual or contextual factors. Studies considered to present a probable risk of bias were characterised by two or more of the risks identified above. Differences in ratings between coders were discussed in joint meetings.

Data extraction

A coding sheet was developed to identify: study authors, place of study, type of policy change/ study period, participant characteristics (ns), study design, cannabis use measure, statistical methods used/covariates controlled for, key findings and risk of bias.

Meta-analysis

To meta-analyse the effects of the liberalisation of cannabis policy on levels of use, we calculated Standardised Mean Differences (SMD) and associated 95% confidence intervals for each finding using the Practical Meta-Analysis Effect Size Calculator[18]. Effects sizes from

different studies were combined into a weighted mean effect size. Each effect size was weighted by the inverse of its variance and then averaged[19]. Standard meta-analytical procedures suppose the independence of effects[20]. However, several primary studies provided multiple correlated effect size estimates for the same underlying outcome (e.g. 30-day use, 12-month use etc.). To avoid the loss of information resulting from the selection of only one effect size per study, we used the Robust Variance Estimation (RVE) method[21], which makes it possible to handle statistically dependent effect sizes. A fixed effect meta-analysis was undertaken in the absence of significant heterogeneity, otherwise a random effects model was used [22]. To test for homogeneity, we computed the Q statistic to determine whether each set of effect sizes shared a common population effect size[19]. To interpret between-study heterogeneity, we used the I^2 statistic; an I^2 <= 50% is generally considered to indicate low heterogeneity[23].

To study whether cannabis use in adolescents and young adults varied as a function of 1) cannabis decriminalisation, 2) legalisation of cannabis use for medical purposes or 3) legalisation of cannabis use for recreational purposes, we conducted three main meta-analyses.

For each type of cannabis policy change, we also performed a priori hypothesised subgroup analyses, according to study design (cohort vs. cross-sectional), study year (< 2000 vs. ≥ 2000), participants' age (< vs. ≥ 18 years) and the measure of cannabis use (30-day use vs. 12-month use). Studies included in this review did not present stratified results based on whether participants were < vs. ≥ 21 years (the legal age for cannabis use in US states which legalised the substance), making it impossible for us to conduct sensitivity analyses using this age cut-off.

Finally, because the results of a meta-analysis can be biased by studies with non-significant results being less likely to be published, we examined publication bias graphically, using a funnel plot. All analyses were performed using STATA 14.0 and the *robumeta* macro [24].

Results

The study flowchart (**Figure 1**) shows our search strategy which resulted in the identification of 41 original research reports to be analysed.

The 41 studies analysed were all published in English: 33 were conducted in the United States[25-57], 3 in Australia[58-60], 2 in the United Kingdom[61 62], 1 in the Netherlands[63], 1 in the Czech Republic[64], and 1 internationally[65]. Thirteen studies evaluated the consequences of cannabis decriminalisation[25-28 37 58-65], 20 the consequences of legalisation of use for medical purposes[29-36 38-45 49 53-55], and 8 the consequences of legalisation of use and possession for recreational purposes[46-48 50-52 56 57]. All studies examining the effects of cannabis legalisation (for medical or recreational purposes) were based in the United States.

The reports included were heterogeneous in terms of the populations studied: 21 focused on adolescents (12-17 years)[25 28 31 33-35 38 41-44 46-50 53 55 56 61 65], 6 on young adults (18-25 years)[37 40 52 57 58 60] and 14 included data on both of these groups[14 26 27 29 30 32 36 39 45 51 58 61-63].

Among studies conducted in the United States, 9 were based on the National Study on Drug Use and Health conducted by the Substance Abuse and Mental Health Services Administration (NSDUH https://nsduhweb.rti.org/respweb/homepage.cfm)[14 31 32 36 39 42-45], 7 on the Monitoring The Future study (MTFS http://monitoringthefuture.org/)[25 28 37 38 41 50 54], 4 on the Youth Behavioral Risk Surveillance survey (YBRS https://www.cdc.gov/healthyyouth/data/yrbs/index.htm)[33-35 49] and 4 on the National

Longitudinal Study of Youth (NLSY79 https://www.nlsinfo.org/content/cohorts/nlsy79[26 27], and NLSY97 https://www.nlsinfo.org/content/cohorts/nlsy97[33 40].

Among studies conducted in Australia, 2 were based on the National Drug Strategy Household Survey (NDSHS http://data.gov.au/dataset/national-drugs-strategy-household-survey).

Thirty four studies were based on repeated cross-sectional data[25 28 29 31-39 41-45 48-60 62-64], 6 on longitudinal cohort data[26 27 40 46 47 61] and one on analyses of routine administrative data[30]. Sample sizes in individual studies ranged from n=336[30] to > 11,703,100[35].

Overall, 16 studies were characterised by a very low risk of bias[14 31 32 34-36 38 41 44 45 49 50 54 58 59 63] and 9 by a low risk of bias[26 27 30 47 48 51-53 55]; in our systematic review only the results of these investigations were analysed. Given the small number of articles in each category, all studies except those with a high level of bias were meta-analysed. In additional analyses, we verified that findings were stable when studies characterised by probable bias were excluded.

Decriminalisation of cannabis use

As shown in **Table 1**, mong the 13 studies examining the consequences of cannabis decriminalisation, three were characterised by a very low risk of bias[58 59 63]. Two of these - one based in Australia (n=15,468) and the second in the Czech Republic (n=1524), and both conducted among adolescents and young adults, found no evidence of statistically significant changes in patterns of cannabis use following policy change[58 63]. However, one study - based in Australia and conducted exclusively among adolescents aged 12-17 years (n=39,0387) - observed a 12% increase in use following cannabis decriminalisation[59]. We also identified one study characterised by a low risk of bias[26] - conducted in the United States and

focusing on 14-21 year olds (n=12,686) - which observed no statistically significant effect of cannabis decriminalisation on youths' use.

Meta-analysing all 13 studies, we observed an I^2 of 99.5%, indicating high heterogeneity. After excluding studies conducted by Williams & Bretteville-Jensen[59] and Miech et al.[37] (Supplementary Figures 1A & 1B), which appeared to be outliers, the I^2 was reduced to 99.1%, but remained too high to conduct a robust meta-analysis. This was unchanged when the analysis was restricted to cohort study data, study year (< or >= 2000), a particular age group (12-17 or 18-25 years), or recent cannabis use (30 days).

Legalisation of cannabis use for medical purposes

As shown in **Table 2**, twenty studies examined the consequences of the legalisation of cannabis use for medical purposes in the United States from 1996 onwards. Twelve were characterised by a very low risk of bias[31 32 34-36 38 41 44 45 49 54]. Of those, six were based on NSDUH data[14 31 32 36 44 45], three on the YRBS[34 35 49] and three on the MTFS[38 41 54]. Altogether six studies (n ranging from 11,453 to 11,703,100) - all conducted among adolescents - one additionally including youths aged 18-20 years[36] and one additionally including youths aged 18-25 years[45] - found no statistically significant effect of the introduction of medical cannabis laws[34-36 38 44 45]. Three of these studies were based on NSDUH data[36 44 45] and two on the YRBS[34 35]. Importantly, both the NSDUH and the YRBS being repeated cross-sectional surveys, the analytical methods used vary across reports in terms of length of follow-up after policy change (from 1 to 9 years), statistical methods (logistic regression[45], difference-in-differences[35], fixed-effects models[36]), as well as covariates. Still, all studies characterised by a very low risk of bias are adjusted for individual demographic characteristics (age, sex, race) as well as contextual factors (at minima a state identifier and the level of cannabis use prior to policy change). In three studies conducted among adolescents, the legalisation of medical

cannabis was followed by a decrease in use[32 41 49]. These three reports were based on different large datasets (NSDUH[32], MTFS[41] and YRBS[49], with ns ranging from 11,813 to 973,089). Finally, three studies (ns ranging from 11,813 to 973,089) observed an increase in levels of cannabis use among adolescents (under 18 years) living in a state which passed medical cannabis laws[14 31 54] and one of these observed a similar effect among young adults (ages 18-25 years) [14].

Two studies were characterised by a low risk of bias[30 53]. One, based on routine data (Arrestee Drug Abuse Monitoring system – ADAM, n=336), showed no statistically significant differences in the prevalence of cannabis use (as ascertained by urine tests) among persons seen in hospital emergency departments before and after medical cannabis laws[30]. The second study reported that among cannabis users recruited via social media (n=2,630), the level of cannabis vaping and eating varied with the time since legalisation of medical cannabis – the longer the time since legalisation, the higher the likelihood of use[53].

Importantly, these data indicate that the provisions of laws enabling access to cannabis for medical purposes, such as the amount of cannabis that individuals are allowed to possess and use, the existence of patient registries[49], the proportion of dispensaries per inhabitant, the authorisation of home cultivation, or concomitant laws making it legal to use cannabis for recreational purposes[53] are influential and should be systematically reported by researchers examining the effects of cannabis policies.

Meta-analysing all 20 studies, we observed an I^2 of 100%, indicating high heterogeneity. After excluding the studies conducted by Wen et al.[36] and Harper et al.[32], which appeared to be outliers (Supplementary Figures 2A & 2B), the I^2 was reduced to 98.6%, but remained too high to conduct a robust meta-analysis. This was unchanged when

the analysis was restricted to cohort studies, study year (< or >= 2000), a particular age group (12-17 or 18-25 years), or recent cannabis use (30 days).

Legalisation of cannabis for recreational purposes

As shown in **Table 3**, We identified 8 studies examining the impact of recreational cannabis laws, which make it legal to use and possess small amounts of cannabis, on youths. They were all conducted in the United States, where several states have introduced this form of cannabis legalisation since 2012. Four studies were based in Washington state[46 47 48 52], two in Colorado[56 65], one in Washington state and Colorado[50] and one in Oregon[51]. Only one study - based on the MTFS - was characterised by a very low risk of bias[50]. This investigation (n=253,902) reported a statistically significant increase in cannabis use among adolescents living in Washington state (3.2% increase among 8th graders and 5.0% increase among 10th graders), but not among those living in Colorado.

We also identified two studies characterised by a low risk of bias. One (n=13,335) reported a 2.0-3.5% increase in the frequency of cannabis use among college students living in Washington state[52] and the other an increase of .02% among middle and high school students living in Colorado (n=24,171)[65].

Meta-analysing all 8 studies, we observed an I^2 of 89.8%, indicating high heterogeneity (Supplementary Figures 3A & 3B). After excluding the study conducted by Cerda et al.[50], which appeared to be an outlier, the I^2 was reduced to 45.0%. This analysis yielded an average standardised mean difference of 0.03 (95% CI -0.01-0.07), suggesting a possible small increase in the use of cannabis following the legalisation of recreational cannabis.

Discussion

Main findings

Our systematic review of studies examining the impact of the liberalisation of cannabis legislation on patterns of use among adolescents and young people, identified 41 reports published prior to March 2018, 16 characterised by a very low risk of bias and 9 by a low risk of bias. With the exception of one study, high quality reports examining the impact of cannabis decriminalisation (n=4) show no statistically significant change in youths' patterns of use. Similarly, the legalisation of cannabis use for medical purposes, extensively evaluated in the United States, does not appear to have an effect: 6 studies suggest no change in cannabis use among youths, 3 studies observe a decrease, and 4 studies report an increase. However, the legalisation of cannabis for recreational purposes, examined in 6 studies with a very low or low risk of bias, may be associated with a small increase in levels of use among youths.

Overall, policies regarding cannabis use and possession seem to have little effect on actual patterns of use among young people, with the possible exception of the legalisation of recreational use. To date, evidence regarding the impact of the legalisation of recreational cannabis comes from the United States, where prevalence levels of substance use are high and laws liberalising cannabis use tend to be market-oriented. Additional data from other settings (e.g. Uruguay, Canada) will help gain a better understanding of relations between cannabis policy and patterns of use in the population.

Limitations and strengths

Our systematic review and meta-analysis has limitations which need to be acknowledged. First, the specific provisions of laws and policies regulating cannabis and which can influence actual access to the substance[2], vary across settings. For example, decriminalisation can imply different limits on the amount of cannabis that leads to a fine –

e.g. the possession of 15 g of herb or 5 g of resin in the Czech Republic is fined approximately 550 euros[63]; in the Australian Capital Territory (Canberra region) the possession of up to 25 g is fined approximately 100 euros, while in Western Australia (Perth region) the possession of less than 10 g is tolerated but higher quantities can result in a conviction[66]. Similarly, laws allowing the use and possession of cannabis for medical purposes, currently in place in approximately 20 countries (e.g. Australia, Belgium, Spain, Canada and some U.S. states) take different forms. For instance, only the Netherlands and some U.S. states make it possible for individuals to purchase or grow cannabis that can be smoked – in other settings individuals can purchase specific medicines derived from cannabinoids (e.g. the United Kingdom). The legal age at which individuals are authorised to possess cannabis (18 or 21 years) varies across settings, with possibly differential effects on levels of use among young adults. Finally, the price of cannabis, which influences levels of use among young people[58 67], varies from place to place and over time. Clearly, differences in specific policy provisions, which have an impact on cannabis availability, make it difficult to compare different settings. Nevertheless, at the time of its implementation or even before if there is wide media coverage, policy change in and of itself can influence the perceptions of cannabis, which in turn shape levels of use[41], justifying the conduct of this systematic review. Second, the duration of follow-up varies across studies, in part because changes in cannabis policy occurred in different periods and places. This is especially a concern for reports evaluating the impact of recreational cannabis laws: policy changes introduced decades ago (e.g. the Netherlands) were not fully evaluated, while follow-up is limited for more recent policy modifications (e.g. the United States, Uruguay). It is unclear whether the introduction of policies that liberalise cannabis use and possession is most likely to influence patterns of use in the short or in the long-term; in the present report we considered that a follow-up period

of at least one year following actual policy implementation was necessary to test a possible effect. Third, among studies examining the consequences of the legalisation of cannabis for recreational purposes, we only identified one study characterised by a very low risk of bias and 5 by a low risk of bias, and the findings we report will need to be confirmed. Our attempt to meta-analyse the results of different studies included in this review proved inconclusive, with the exception of legalisation of cannabis for recreational purposes: this calls for additional, methodologically robust, studies in this area. Fourth, although changes in cannabis policies have occurred in various settings, most studies included in this report were conducted in the United States, where most research in this area has been conducted. It is difficult to assess the extent to which the findings observed in the U.S. will generalise to other countries, and it will be important to update knowledge in this area once data from other places (e.g. Uruguay, Canada) become available.

Despite these limitations, our study has several strengths: a) the evaluation of studies published in different disciplines (public health, epidemiology, economics, social policy) through multiple databases; b) the combination of data from different settings (United States, Australia, Europe); c) special attention to the risk of bias, examined using a framework especially developed for observational studies. Moreover, our systematic review takes into consideration different forms of liberalisation of cannabis policies (decriminalisation, legalisation for medical purposes and for recreational purposes), attempting to tackle this complex issue in a thorough way.

Methodological issues

The studies included in this systematic review relied on several different datasets and applied quite varied methods (logistic regression[45], difference-in-differences[35], fixed-effects

models[36]), to isolate the effects of policy change on patterns of cannabis use independently of individual and contextual characteristics; such triangulation of different methods is considered especially reliable when, as in this case, it yields consistent results[68]. Importantly, because cannabis policy changes most often occur in settings where public support and levels of use are high, it is essential to take into account levels of cannabis use prior to policy change, as was the case in all reports we considered to present a very low or low risk of bias. Finally, it is important to note that we evaluated relative changes in cannabis use post vs. pre policy change. Levels of cannabis use vary widely across settings and in some places may have been so high prior to policy change that additional increases are unlikely (this may be the case of Colorado where over 25% of 12th graders use cannabis on a monthly basis)[50].

Most studies included in our systematic review were cross-sectional, because reports based on longitudinal data are less numerous and were not always of sufficiently high quality. While repeated cross-sectional studies are well-suited to examine long-term changes in patterns of cannabis use in relation to changes in the legal context, additional evidence from longitudinal data following young people would make it possible to take into account individual characteristics and further strengthen the inference that can be drawn regarding the impact of cannabis policy change.

Implications

Summarising the available evidence, we found that, contrary to what has been observed in adults[36 58 69], cannabis decriminalisation and legalisation for medical purposes are probably not related to significant changes in patterns of use among adolescents and young people. This was also recently reported by a systematic review and meta-analysis which focused on medical cannabis laws and patterns of use in the preceding 30 days among adolescents[70]. On the other hand, the legalisation of cannabis use for recreational purposes may lead to higher

levels of use in this age group and a younger age at initiation. Several hypotheses have been proposed to explain this multifactorial phenomenon: a) changes in the reporting of cannabis use; b) a decrease in perceived harmfulness[41]; c) an increase in cannabis availability and access; d) a decrease in price (in legal outlets or on the black market)[71]. While the liberalisation of cannabis policy can have both collective and individual benefits (e.g. decrease in costs of law enforcement, increase in quality control, reduction in individuals' difficulties with the legal system), these data suggest the possibility of small negative public health implications. Adolescents and young adults are especially vulnerable to the consequences of cannabis use, in terms of both biological and social development[72 73], therefore policies that involve the legalisation of recreational use of cannabis need to be accompanied by prevention efforts targeted towards young people. The most effective prevention programs aim to improve school climate and strengthen youths' psychosocial skills such as self-esteem and conflict resolution[74 75].

Conclusion

In recent decades, cannabis policies have been liberalised in different ways (decriminalisation, legalisation of use for medical or recreational purposes) and in various settings. Our systematic review and meta-analysis of 41 research articles published across disciplines (epidemiology, economics, social policy) and using a variety of datasets and statistical methods shows that cannabis decriminalisation or legalisation of use for medical purposes do not result in higher levels of use among youths. Legalisation of use for recreational purposes appears to possibly result in a small increase. It will be important to reassess whether this tendency persists over time, varies across subgroups of youths (male vs. female, urban vs. rural, socioeconomically disadvantaged vs. favoured), and is comparable across settings, particularly as additional countries introduce changes in

cannabis policy (e.g. Canada). Repeated cross-sectional as well as longitudinal studies will be necessary to thoroughly evaluate adolescents' levels of cannabis use following changes in policy.

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Figure legend: Figure 1. Flowchart showing the screening and selection process of articles selected for the study of the impact of liberalisation of cannabis policy with regard to levels of use in adolescents and young adults.

Table 1. Studies examining cannabis use levels in adolescents before and after decriminalisation of cannabis possession (1981-2017).

	Study	Place of study	Type of policy change/study period	Participant characteristics / n	Study design	Cannabis use measures (frequency/ period)	Statistical methods/ covariates	Key findings/effect size	Risk of bias[1] (/10)
1	Johnston et al., 1981[25]	California, Maine, Minnesota, Ohio (early change) + North Carolina, New York, Missouri (late change) vs. states with no decriminalisation	Decriminalisation of cannabis possession in 1975 and 1976	12th grade students participating in the Monitoring the Future surveys (MTFS)/ n~99,000 per year	Cross-sectional survey (1975-1980)	12 months, 30 day, and daily use	Comparisons of prevalence rates	12-month use: d=0.06, 95% CI 0.0003; 0.127; 30-day use: d=0.125, 95% CI 0.059; 0.191(unadjusted)	R1: 8 R2: 8.1 Average: 8.1 Possible
2	Thies & Register, 1993[26]	Alaska, California, Colorado, Maine, Minnesota, Missouri, Nebraska, New York, North Carolina, Ohio, Oregon	Decriminalisation of cannabis possession 1976-1979	14-21 year olds participating in the National Longitudinal Survey of Youths1979 (NLSY) /n=12,686	Cohort study with follow-up in 1984 and 1988.	30 day use	OLS regression models controlled for sex, race, parental education, own education, income, church attendance, marital status, urban setting; legal context regarding underage drinking	1984: d=0.05, 95% CI -0.02; 0.14; 1988: d=0.06, 95% CI -0.03; 0.16 (unadjusted)	R1: 9 R2: 9 Average: 9 Low
3	McGeorge & Aitken, 1997[58]	Australian Capital Territory vs. Melbourne	Decriminalisation of cannabis possession, use and cultivation in 1992	3rd year university students at Australian National University and Melbourne University /n=903	Cross-sectional survey (1994)	12-month use	Chi-square statistics	d=0.21, 95% -0.02; 0.45 (unadjusted)	R1: 6.4 R2: 4.5 Average: 5.5 Probable
4	MacCoun, 1997[63]	Netherlands	Decriminalisation of cannabis in	16-18 year olds participating in a	Repeated cross-sectional	Lifetime use	Comparison of prevalence rates	Netherlands vs. US: d=-0.23; 95% CI -0.26; -	R1: 8.1 R2: 8.2

[1] R1 : Rater 1 ; R2 : Rater 2

			1976 followed by legalisation in 1984	school-based survey (Trimbos) vs. Youths of the same age in the US (Monitoring the Future)/ n~115,000	surveys: 1970 to 1996			0.19 (unadjusted)	Average: 8.2 Possible
5	Pacula 1998[27]	Alaska, California, Colorado, Maine, Minnesota, Missouri, Nebraska, New York, North Carolina, Ohio, Oregon	Decriminalisation of cannabis possession 1976-1979	14-21 year olds participating in the National Longitudinal Survey of Youths1979 (NLSY)/n=8,008	Cohort study with follow-up in 1984.	30 day use	Two part model controlled for sex, age, race, number of siblings, urban setting, academic achievement, expected years of schooling, illegal activity; parents' marital status, employment status, alcohol use; legal context regarding alcohol use, crime level, beer and cigarette taxes	d=0.0179, 95% CI -0.038; 0.0008	R1: 10.0 R2: 8.1 Average: 9.1 Low
5	DiNardo & Lemieux 2001[28]	California, Colorado, Maine, Minnesota, Mississippi, Nebraska, New York, North Carolina, Ohio, Oregon	Decriminalisation of cannabis possession 1976-1979	12th grade students participating in the Monitoring the Future surveys (MTF) /n~165,000	Cross-sectional survey (1980-1989)	30 day use	Structural regression model controlled for sex, age, race, parental education, weekly hours of work, income, alcohol use, state-level unemployment and alcohol drinking age	d=-0.08, 95% CI -0.12; -0.05	R1: 7.7 R2: 7.7 Average: 7.7 Possible
7	Williams 2004[59]	Australian Capital Territory, Northern Territory vs. non decriminalising states	Decriminalisation of cannabis possession, use and cultivation between 1988 and 1998	14-25 years , Australian National Drug Strategy Household Survey (NDSHS)	Repeated cross-sectional surveys (1988, 1991, 1993, 1995, 1998)	12-month use	Ordered probit model controlled for sex, age, marital status, dependent children, ethnicity, educational level,	d=0.04, 95% CI -0.102; 0.192	R1: 9.2 R2: 10 Average: 9.6 Very low

				/n=15,468			employment, capital city residence, decriminalisation regime		
8	Williams & Bretteville-Jensen, 2014[60]	South Australia, Australian Capital Territory, Northern Territory, Western Australia vs. non-decriminalising states	Decriminalisation of cannabis possession, use and cultivation between 1987 and 2004.	20-40 year old lifetime users of cannabis participating in the Australian National Drug Strategy Household Survey (NDSHS) /n=39,087	Repeated cross-sectional surveys (1998, 2001, 2004, 2007, 2010)	Age at initiation	Difference-in-differences with discrete time hazard model controlled for sex, education, ethnicity, capital city residence, survey year	12-17 years: d=0.57, 95% CI 0.52; 0.63	R1: 10 R2: 10 Average: 10 Very low
9	Fuller, 2014[61]	England	Declassification of cannabis from schedule B to schedule C drug (2004) and then back (2009)	11-15 year olds participating in a representative school survey/n=6,173	Repeated cross-sectional surveys (2001-2014)	12-month use	Prevalence rates	2004 vs. 2009: d=-0.22, 95% CI -0.29; -0.165 (unadjusted)	R1: 6.4 R2: 6.4 Average: 6.4 Probable
10	Braakmann & Jones, 2014[62]	United Kingdom	Declassification of cannabis from schedule B to schedule C drug (2004)	15-25 year olds participating in the Offending, Crime and Justice Survey (OCJS)/n=2,539	Cohort study (2003-2006)	12-month and 30-day use;	Difference-in-differences model controlled for age and calendar year	12-month use; 15-17 yrs: d=-0.01, 95% CI -0.07; 0.002; 18-25 yrs: d=-0.05, 95% CI -0.15; 0.05; 30-day use: 15-17 years: -0.006, 95% CI -0.009; 0.08; 18-20 years: -0.13, 95% CI -0.24; -0.02	R1: 8.6 R2: 8.0 Average: 8.3 Possible
11	Miech et al, 2015[37]	California vs. other US states	Decriminalisation in 2010	8th, 10th and 12th grade students participating in the Monitoring the Future surveys (MTF)/n=97,238	Repeated cross-sectional surveys (2007-2012)	12-month and 30-day use	GEE regression models	12-month: d=0.32, 95% CI 0.31-0.34; 30-day use: d=0.57, 95% CI 0.55-0.59 (unadjusted)	R1: 8.6 R2: 9.0 Average: 8.8 Possible
12	Shi et al, 2015[65]	Cross-national study of 38 countries	Depenalisation, decriminalisation, and partial	15 year olds participating in the Health	Repeated cross-sectional surveys	12-month and regular (>=40 times in	Multilevel logistic random intercept regression	12-month use: d=-0.004, 95% CI -0.02; 0.13; regular use:	R1: 8.2 R2: 8.0 Average:

			prohibition changed since 0-5 years, 5-10 years or >10 years	Behaviour in School-Aged Children Study (HBSC)/ n=172,894	(2001/2002, 2005/2006, 2009/2010)	lifetime) use		d=0.17, 95% CI 0.13; 0.20	8.1 Possible
13	Červený J et al, 2017[64]	The Czech Republic	Decriminalisation of cannabis possession in 2010	15-25 years participating in drug use monitoring surveys/ n=1086 in 2008 and 438 in 2012	Repeated cross-sectional surveys (2008-2012)	Age at initiation	Mixed proportional hazards controlled for sex, education, birth cohort and region of residence	d=-0.26, 95% CI -0.37; -0.15 (unadjusted)	R1: 10 R2: 10 Average: 10 Very low

Table 2. Studies examining cannabis use levels in adolescents before and after the legalisation of cannabis use for medical purposes (1996-2018).

	Study	Place of study	Type of policy change/study period	Participant characteristics / n	Study design	Cannabis use measure (frequency/ period)	Statistical methods/ covariates	Key findings/effect size	Risk of bias (/10)[1]
1	Khatapoush & Hallfors, 2004[29]	California (CA)	State-level Medical marijuana laws (MML): Proposition 215 (1996)	16-25 year olds participating in the Robert Wood Johnson Foundation's Fighting Back initiative (FB)/n=2,651	Repeated cross-sectional surveys in 1995, 1997 and 1999.	12-month and 30-day use	Logistic regression model	12-month use: d=0.54, 95% CI 0.48; 0.59; 30-month use: d=0.72, 95% CI 0.64; 0.79 (unadjusted)	R1: 8.6 R2: 8.0 Average: 8.3 Probable
2	Gorman et al, 2007[30]	Los Angeles, San Diego, San Jose (CA), Portland (OR)	State-level Medical marijuana laws (MML) introduced before 2002	10-18 year olds registered in the Arrestee Drug Abuse Monitoring system (ADAM)/ on average n=255 in California & n=81 in Oregon	Routine data collection (1995-2002)	Urine test data (>=50 ng of THC per decilitre)	Interrupted time series design	California: 10-18 yrs: d=-0.42, 95% CI -0.60; -0.24; Oregon: 10-18 yrs: d=-0.75, 95% CI -1.33; -0.17 (unadjusted)	R1: 9.2 R2: 9.1 Average: 9.2 Low
3	Wall et al, 2011[31]	Alaska, California, Colorado, Hawaii, Maine, Nevada, Oregon, Washington + Michigan, Montana, New Mexico, Rhode Island, Vermont + Arizona, Delaware, New Jersey vs. other US states	State-level Medical marijuana laws (MML) introduced before 2002	12-17 olds participating in the National Survey of Drug Use and Health (NSDUH)/ n~11,813	Repeated cross-sectional surveys (2002-2008)	30-day use	Fixed effects model with random intercept, controlled for cannabis use 2002-2008	2002-2003: d=0.15, 95% CI 0.07; 0.23	R1: 9.7 R2: 9.4 Average: 9.6 Very low

[1]R1 : Rater 1 ; R2 : Rater 2

4	Harper et al, 2012[32]	Alaska, California, Colorado, Hawaii, Maine, Nevada, Oregon, Washington + Michigan, Montana, New Mexico, Rhode Island, Vermont vs. other US states	State-level Medical marijuana laws (MML) introduced before 2002	12-17 year olds and 18-25 year olds participating in the National Survey of Drug Use and Health (NSDUH) /n~11,813 per age group	Repeated cross-sectional surveys (2002-2009)	30-day use	Difference-in-differences estimates controlled for measurement error	12-17 years: d=-1.25, 95% CI –1.29; -1.21; 18-25 years: d=1.71, 95% CI 1.67 - 1.75	R1: 9.4 R2: 9.5 Average: 9.5 Very low
5	Anderson et al, 2012[33]	Alaska, Arizona, California, Colorado, Delaware, District of Columbia, Hawaii, Maine, Michigan, Montana, Nevada, New Jersey, New Mexico, Oregon, Rhode Island, Vermont, Washington vs. other US states	State-level Medical marijuana laws (MML) introduced before 2011	15-19 years olds participating in the National and State Youth Risk Behavior Surveys (YRBS) /n=786,568	Repeated cross-sectional surveys (1993-2011)	30-day use; 30-day frequent use;	Linear regression controlled for age, sex, race, grade, state-level marijuana decriminalisation, BAC 0.08 laws, state beer tax, income per capita, unemployment	YRBS: 30day use: d=-0.32, 95% CI -0.33; -0.32; 30-day frequent use d=-0.18, 95% CI -0.19; -0.18	R1: 8.5 R2: 8.1 Average: 8.3 Possible
6	Lynne-Landsman et al, 2013[34]	Delaware, Michigan, Montana, Rhode Island compared pre and post-MML implementation	State-level Medical marijuana laws (MML) introduced 2003-2009	9-12th graders participating in the Youth Risk Behavior Surveys (YRBS) /n~11,453	Repeated cross-sectional surveys (2003-2009)	30-day use;	Difference in differences controlled for age, ethnicity, and sex	d=0.24, 95% CI 0.20;0.28	R1: 9.2 R2: 10 Average: 9.6 Very low
7	Choo et al, 2014[35]	Idaho vs. Montana, Massachusetts vs. Rhode Island, New Hampshire vs. Maine, Utah vs. Nevada, New York vs. Vermont	State-level Medical marijuana laws (MML)	9-12th graders participating in the Youth Risk Behavior Surveys (YRBS)/ n~11,703,100	Repeated cross-sectional surveys since 1991, 1993, 1995, 1997, 1999, 2001, 2003, 2005, 2007	30 day use	Difference-in-differences controlled for state, year, age, sex, race, grade	d=0.065, 95% CI 0.026; 0.105	R1: 10 R2: 9.5 Average: 9.8 Very low
8	Wen et al, 2014[36]	District of Columbia,	State-level Medical	12-20 year olds participating in	Repeated cross-sectional	30-day use;	Fixed-effects models controlled	d=-1.72, 95% CI:-1.73;-1.71	R1: 9.6 R2: 10

		Michigan, Montana, New Jersey, New Mexico, Rhode Island, Vermont vs US states with no MML laws by 2010	marijuana laws (MML) introduced between 2004 and 2010	the National Survey on Drug Use and Health (NSDUH)/ n~183,600	surveys (2004-2011)		for age, sex, race, self-reported health, cigarette use, urban residence, family poverty, state-level unemployment, mean income, median income, alcohol excise taxes.		Average: 9.8 Very low
9	Hasin et al, 2015[38]	21 US states that passed MML vs. non-MML US states	State-level Medical marijuana laws (MML) introduced by 2014	8th, 10th and 12th grade (13, 15, 17) students participating in the Monitoring the Future surveys (MTF) /n=1,098,070	Repeated cross-sectional surveys (1991-2014)	30-day use;	Multilevel regression models controlled for sex, age, race, parental education, class size, private school, urban setting, state-level proportion of males, whites, persons with no high school education and aged 11-24 years	d=-0.033, 95% CI -0.039; -0.026	R1: 10 R2: 10 Average: 10 Very low
10	Schuermeyer et al, 2015[39]	Colorado vs. 34 non-MML US states	State-level Medical marijuana laws (MML) introduced in 2009	12-20 year olds participating in the National Survey on Drug Use and Health (NSDUH)/ n~158,600 12-17 year olds + 159,200 18-25 year olds	Repeated cross-sectional surveys (2006-2011)	>=20 times in 30-days use	Logistic regression controlled for state, year, age, sex, race, educational level and state-by-year interaction	12-17 yrs: d=0.09, 95% CI -0.04 ; 0.23; 18-25 yrs: 0.23, 95% CI 0.16-0.29 (unadjusted)	R1: 9 R2: 8.2 Average: 8.6 Possible
11	Pacula et al, 2015[40]	Alaska, Arizona, California, Colorado, Delaware, District of Columbia,	State-level Medical marijuana laws (MML) introduced before	- <21 year olds participating in the National Longitudinal Survey of	Cohort study (1997-2011)	30-day use;	Difference-in-differences models controlled for population unemployment	d=-0.0109, 95% CI, -0.03; 0.009	R1: 8.2 R2: 8.6 Average: 8.4 Possible

		Hawaii, Maine, Maryland, Michigan, Montana, Nevada, New Jersey, New Mexico, Oregon, Rhode Island, Vermont, Washington vs. US states with no MML in 2012	2012; comparison of different legal provisions: patient registry; home cultivation; legal dispensaries;	Youths1997 (NLSY)/46,375			rate, age distribution, state beer tax rate, BAC 0.08 tax;		
12	Keyes et al, 2016[41]	21 US states that passed MML vs. non-MML US states	State-level Medical marijuana laws (MML) introduced by 2014	8th, 10th and 12th grade (13, 15, 17) students participating in the Monitoring the Future surveys (MTF) /n=973,089	Repeated cross-sectional surveys (1991-2014)	30-day use;	Time-varying multilevel regression models controlled for sex, age, race, parental education, class size, private school, urban setting, state-level proportion of males, whites, persons with no high school education and aged 11-24 years	d=-0.03, 95% CI -0.03;-0.027	R1: 9.6 R2: 9.5 Average: 9.6 Very low
13	Maxwell & Mendelson, 2016[42]	California, Colorado and Washington vs. other US States	State-level Medical marijuana laws (MML) and Recreational marijuana laws (RML)	12-25 year olds participating in the National Survey of Drug Use and Health (NSDUH)	Repeated cross-sectional surveys (2002-2013)	12-month use	Comparison of prevalence rates	Impossible to calculate	R1: 5 R2: 6.8 Average: 5.9 Probable
14	Stolzenberg et al, 2016[43]	Alaska, Arizona, California, Colorado, Delaware, Hawaii, Maine, Michigan, Montana, Nevada,	State-level Medical marijuana laws (MML) introduced between 1998 and 2011	12-17 olds participating in the National Survey of Drug Use and Health (NSDUH) /n~112,500	Repeated cross-sectional surveys (2002-2011)	30-day use	Random effects model controlled for state-level medical cannabis possession limit, cannabis availability, %	d=0.060, 95% CI 0.034;0.087	R1: 7.3 R2: 8.1 Average: 7.7 Possible

		New Jersey, New Mexico, Oregon, Rhode Island, Vermont, Washington vs. other US states					enrolled in drug class, alcohol use, prior crime conviction, % families on income assistance, % juveniles who skipped school, % families where the father resides in household, % male, % white		
15	Wall et al, 2016[44]	Arizona, Delaware, Michigan, Montana, New Jersey, New Mexico, Rhode Island, Vermont vs. other US states	State-level Medical marijuana laws (MML) introduced between 2004 and 2011	12-17 olds participating in the National Survey of Drug Use and Health (NSDUH) /n~112,500	Repeated cross-sectional surveys (2002-2011)	30-day use	Fixed effects model	d=-0.0059, 95% CI -0.030;0.018	R1: 9.4 R2: 10 Average: 9.7 Very low
16	Martins SS et al, 2016[45]	Arizona, Connecticut, Delaware, Illinois, Massachusetts, Michigan, New Hampshire, New Jersey, New Mexico, Rhode Island vs. other US states	State-level Medical marijuana laws (MML) introduced between 2005 and 2013	12-17 and 18-25 year olds participating in the National Survey of Drug Use and Health (NSDUH)/ n=175,000 12-17 year olds and 175,000 18-25 year-olds	Repeated cross-sectional surveys (2004-2013)	30-day use	Multilevel logistic regression controlled for sex, ethnicity, insurance status, household income, population density, state proportions of sex, ethnicity, youths, education, unemployment, median household income	12-17 yrs: d=0.02, 95% CI -0.04-0.08; 18-25 yrs: d=0.006, 95% CI -0.035 ; 0.047).	R1: 9.1 R2: 10 Average: 9.6 Very low
17	Johnson et al, 2017[49]	Alaska, Arizona, Colorado, Delaware, Maine, Michigan, Montana, Nevada, New Jersey, New Mexico, Rhode Island, Vermont vs.	State-level Medical marijuana laws (MML) introduced between 1998 and 2011	9-12th graders (14-17) participating in the Youth Risk Behavior Surveys (YRBS) /n=715,014	Repeated cross-sectional surveys (1991-2011)	30-day use and 30-day heavy use (>=20 times)	Fixed effect multiple logistic regression controlled for year, state, age, sex, ethnicity	30-day use: d=-0.042, 95% CI -0.051;-0.032; 30-day heavy use: d=0.0001, 95% CI -0.018;0.0185	R1: 9.5 R2: 9.5 Average: 9.5 Very low

		other US states							
18	Borodovsky et al, 2017[53]	Alaska, Colorado, District of Columbia, Oregon, Washington vs. 20 US states that did not	Legalisation status: MML or RCCL vs. no legal cannabis law	14-18 year olds recruited online (via targeted Facebook invitations) /n=2,630	Cross-sectional survey (April 29-May 18, 2016)	30-day cannabis use via smoking, vaporizing, or eating.	Logistic and linear regression controlled for age, gender, race, grade level, lifetime days of cannabis use, age of onset.	d=0.064, 95% CI -0.048;0.176	R1: 9.5 R2: 9.1 Average: 9.3 Low
19	Mauro et al, 2017[14]	Arizona, Connecticut, Delaware, Illinois, Maine, Michigan, New Hampshire, New Jersey, New Mexico, Rhode Island, vs. 27 US states with no MML by 2013	State-level Medical marijuana laws (MML) introduced prior to 2015	12-17 and 18-25 year olds participating in the National Survey of Drug Use and Health (NSDUH) /n~175,000 12-17 year-olds and 175,000 18-25 year year olds	Repeated cross-sectional surveys (2004-2013)	State-level 30-day and daily use	Multilevel linear regression controlled for trends in marijuana use and state-level % males, % White, % aged 10-24 years, % > 25 yrs with no high school degree, % unemployed, median household income.	30-day use: 12-17 years: d=0.041, 95% CI 0.022; 0.059; 18-25 years: d=0.016, 95% CI 0.003; 0.029; daily use: 12-17 years: d=-0.003, 95% CI -0.021; 0.014; 18-25 years: d=0.064, 95% CI 0.050; 0.078	R1: 10 R2: 9.5 Average: 9.8 Very low
20	Cerda et al, 2018[10]	Arizona, California, Colorado, Connecticut, Delaware, Illinois, Maine, Maryland, Massachusetts, Michigan, Minnesota, Montana, Nevada, New Hampshire, New Jersey, New Mexico, New York, Oregon, Rhode Island, Vermont, Washington vs. other US states	State-level Medical marijuana laws (MML) introduced prior to 2015; time since legalisation.	8th, 10th and 12th graders (13, 15, 17) participating in the Monitoring the Future Survey/ n=1,140,768	Repeated cross-sectional survey (1991-2015)	30-day use	Difference-in-differences models controlled for individual grade, age, sex, race/ethnicity, socioeconomic status, number of students per grade, public vs. private school, school in metropolitan statistical area, state-level % males, % White, % aged 10-24 years, and % older than 25 with no high school degree.	d=0.0176, 95% CI 0.0170;0.0182	R1: 10 R2: 10 Average: 10 Very low

Table 3. Studies examining cannabis use levels in adolescents before and after legalisation of recreational cannabis use (2016-2018).

	Study	Place of study	Type of policy change/study period	Participant characteristics / n	Study design	Cannabis use measure (frequency/ period)	Statistical methods/ covariates	Key findings	Risk of bias (/10)[1]
1	Estoup et al, 2016[46]	Washington	Legalisation in 2012	High school students (14-17) with problematic substance use enrolled in high school in the Seattle area/ n=262	Cohort study (2010-2015)	3-month use	Mediation model	d=0.061, 95% CI -0.110; 0.232 (unadjusted)	R1: 7.1 R2: 7.4 Average: 7.3 Possible
2	Mason et al, 2016[47]	Washington vs. other US states	Legalisation in 2012	8th graders (14) in Tacoma, WA participating in a longitudinal study/n=238	Cohort study (2010/2011-2012/2013)	30-day use	Multilevel regression models controlled for substance use initiation prior to baseline	d=0.323, 95% CI -0.177; 0.825	R1: 9.2 R2: 9.1 Average: 9.2 Low
3	Fleming et al, 2016[48]	Washington vs. other US states	Legalisation in 2012	10th (16) graders participating in the biennial Washington state school survey/n=30,365	Repeated cross-sectional surveys (2000-2014)	30-day use	Logistic regression analyses controlled for perceived harm of marijuana, alcohol use, and year	d=0.044, 95% CI -0.019; 0.069	R1: 9.2 R2: 9.2 Average: 9.2 Low
4	Cerdá et al, 2017[50]	Colorado and Washington vs. other US states	Legalisation in 2012	13-18 years participating in the Monitoring the Future surveys (MTF)/ n= 253,902	Repeated cross-sectional surveys (2010-2015)	30-day use	Difference-in-differences	d=1.03, 95% CI 1.00; 1.06	R1: 9.1 R2: 10 Average: 9.6 Very low
5	Kerr et al, 2017[51]	2 universities in Oregon vs. 6 in	Legalisation in 2015	18-26 year old college	Repeated cross-sectional	30-day use	Mixed-effects logistic regression	d=0.0139, 95% CI 0.048; 0.075	R1: 9.5 R2: 8.5

[1] R1 : Rater 1; R2 : Rater 2

		other US states		undergraduates participating in the Healthy Minds Study/n=10,924	surveys (2014 and 2016)		controlled for cigarette use, year in college, age, sex, race, residential type, relationship status, sexual orientation, international student status, depression, anxiety, adjustment, institution size and survey period		Average: 9 Low
6	Miller et al, 2017[52]	Washington	Legalisation in 2012; Opening of licensed retail stores for marijuana in 2014	College students participating in the National College Health Assessment (WSU NCHA)/n=13,335	Repeated cross-sectional surveys (2005, 2006, 2008, 2010, 2012, 2014, 2015)	30-day use	Logistic regression controlled for age, sex, race, year in school, estimated secular increase in cannabis use.	Post MML (2014): d=0.04, 95% CI 0.002 ; 0.083; post-RML (2015): d=0.082, 95% CI 0.034 ; 0.130	R1: 9.5 R2: 8.5 Average: 9 Low
7	Harpin et al, 2018[66]	Colorado	Legalisation in 2012	6-12th grade (11-17) students (Healthy Kids Colorado Survey)/n=24,171	Repeated cross-sectional survey (2013 and 2014)	30-day use	Comparison of prevalence rates	d=0.006, 95% CI -0.026; 0.038 (unadjusted)	R1: 9.4 R2: 9.4 Low
8	Jones et al., 2018[57]	Colorado	Legalisation in 2012	College students(22-24 years) n=1,413	Repeated cross-sectional survey (October 2013, March 2014, October 2014 and March 2015)	Lifetime	Comparison of prevalence rates	d=-0.215, 95% CI -0.385; -0.039 (unadjusted)	R1: 4.4 R2: 5.0 Average: 4.7 High

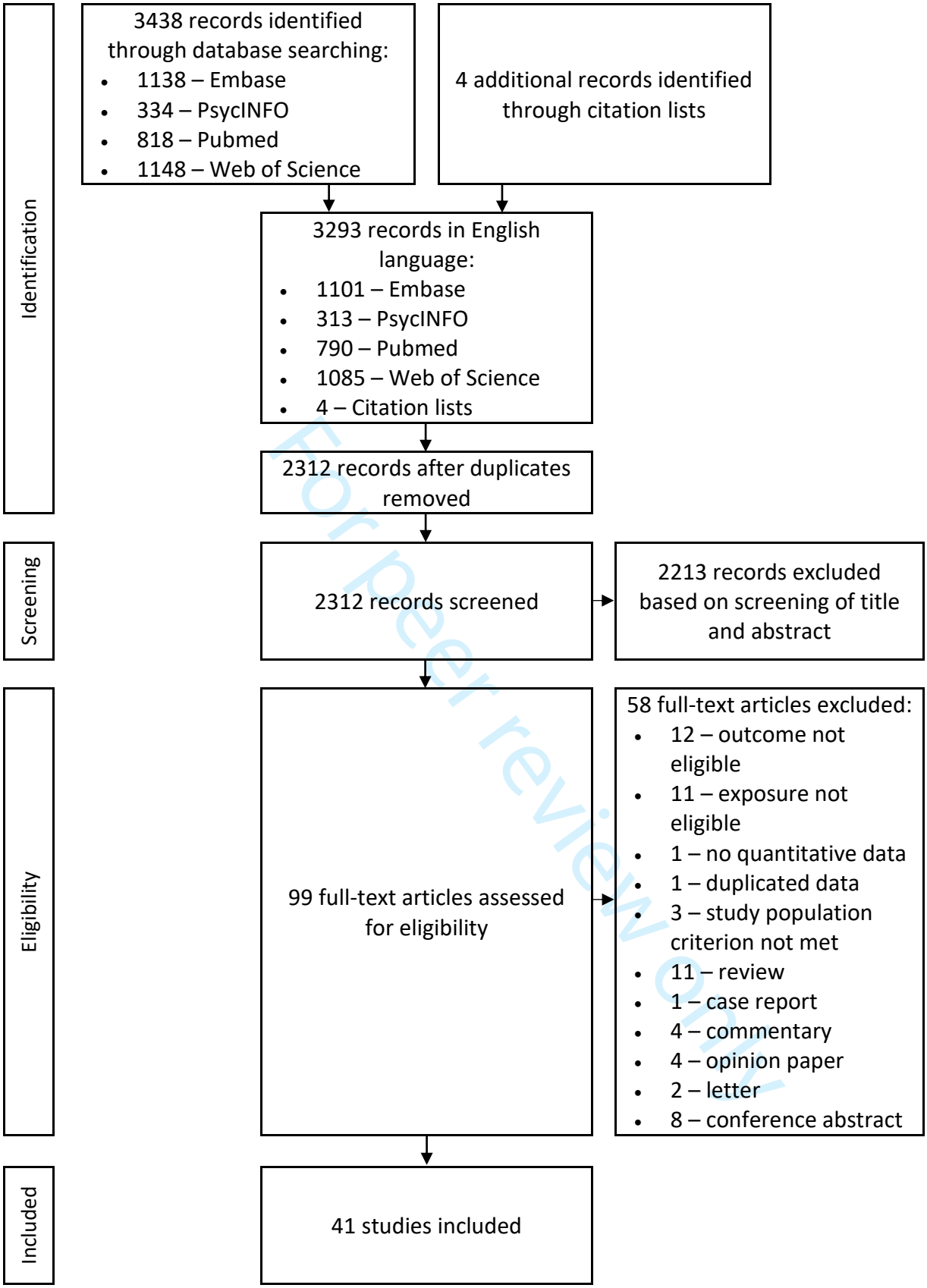


Figure 1. Flowchart showing the screening and selection process of articles selected for the study of the impact of liberalisation of cannabis policy with regard to levels of use in adolescents and young adults.

Supplementary file 1. Full search strategy

Platform: Pubmed

Notes:

1- [MH] indicates MesH Terms
2- [TW] indicates Text Word. Terms that are qualified with this field tag were searched in the following fields: title, abstract, MeSH headings and subheadings, other terms field (which includes author-supplied keywords), secondary source identifier
3- Terms qualified with * were searched with their variations (for different endings)

Search string:

(law*[MH] OR law*[TW] OR decriminalization[MH] OR decriminalization[TW] OR legalization[MH] OR legalization[TW])

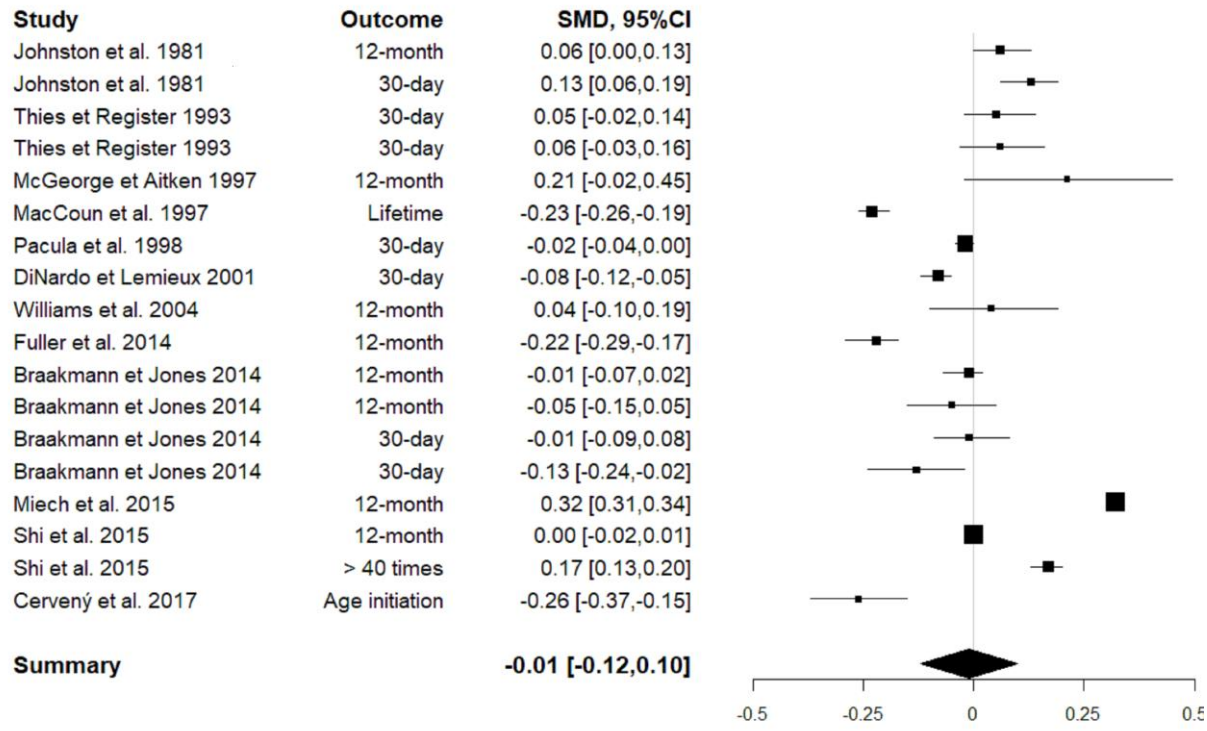
AND

(cannabis[MH] OR cannabis[TW] OR pot[MH] OR pot[TW] OR weed[MH] OR weed[TW] OR marijuana[MH] OR marijuana[TW] OR grass[MH] OR grass[TW])

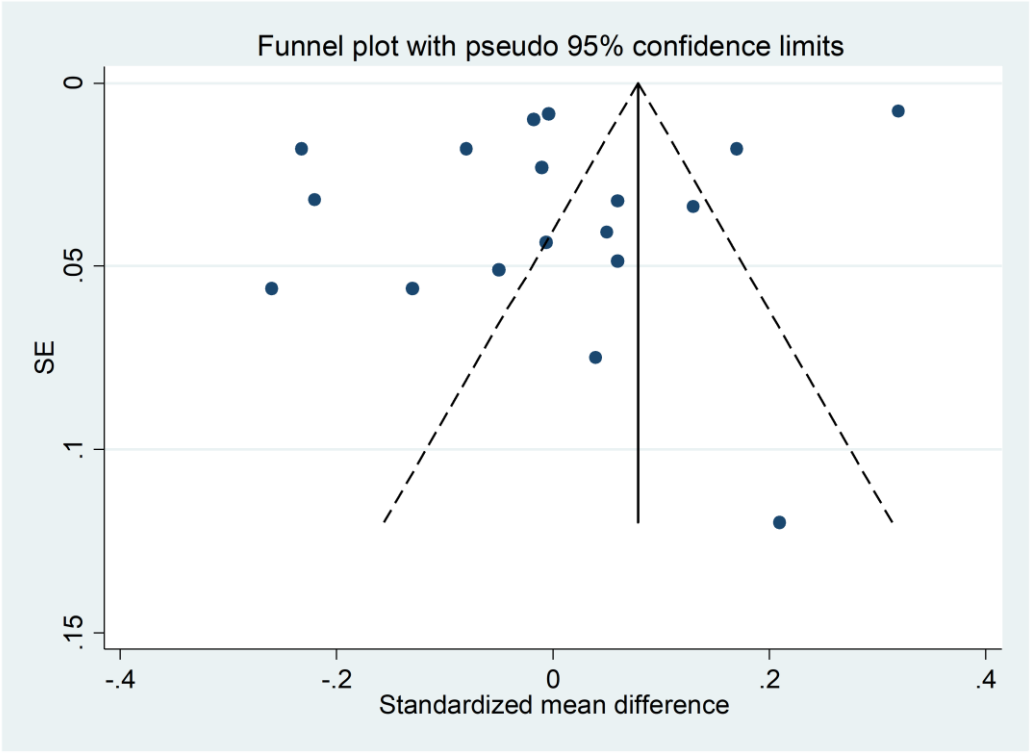
AND

(young[MH] OR young[TW] OR youth[MH] OR youth[TW] OR adolescen*[MH] OR adolescen*[TW] OR teen*[MH] OR teen*[TW] OR school*[MH] OR school*[TW] OR student[MH] OR student[TW])

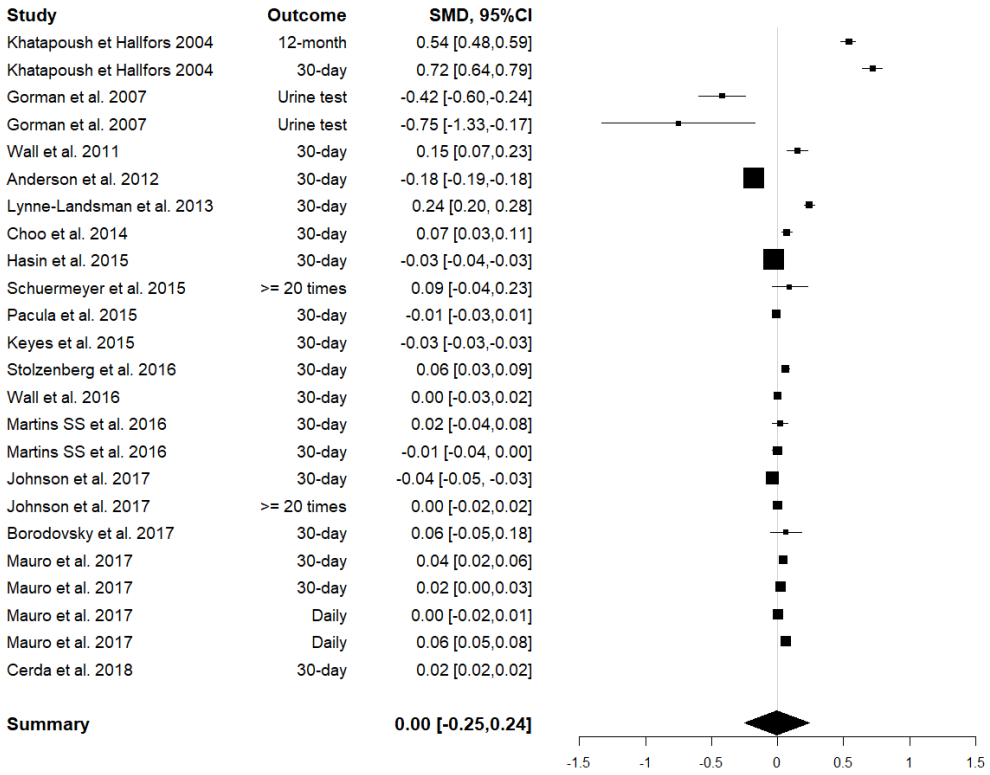
Limits: English language



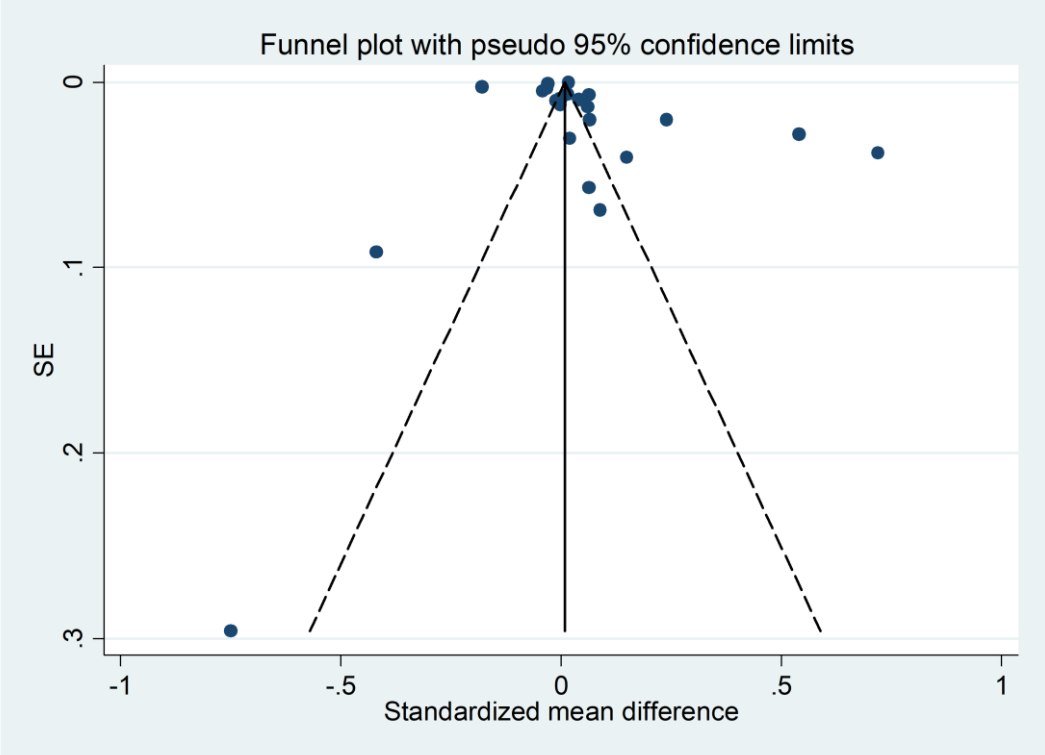
Supplementary Figure 1A: Meta-analysis of studies examining the relationship between cannabis decriminalization and levels of use in adolescents and young adults (12-25 years, prior to March 2018).



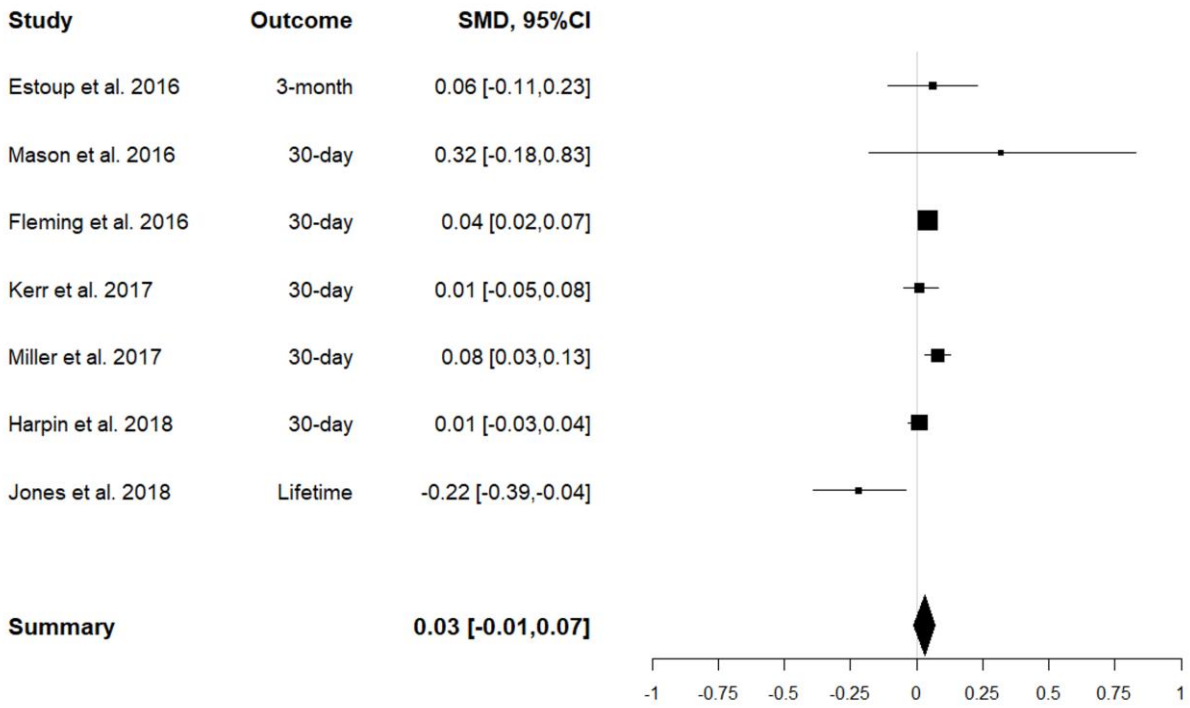
Supplementary Figure 1B: Funnel plot of studies examining the relationship between cannabis decriminalisation and levels of use in adolescents and young adults (12-25 years, I^2=99.1%, prior to March 2018).



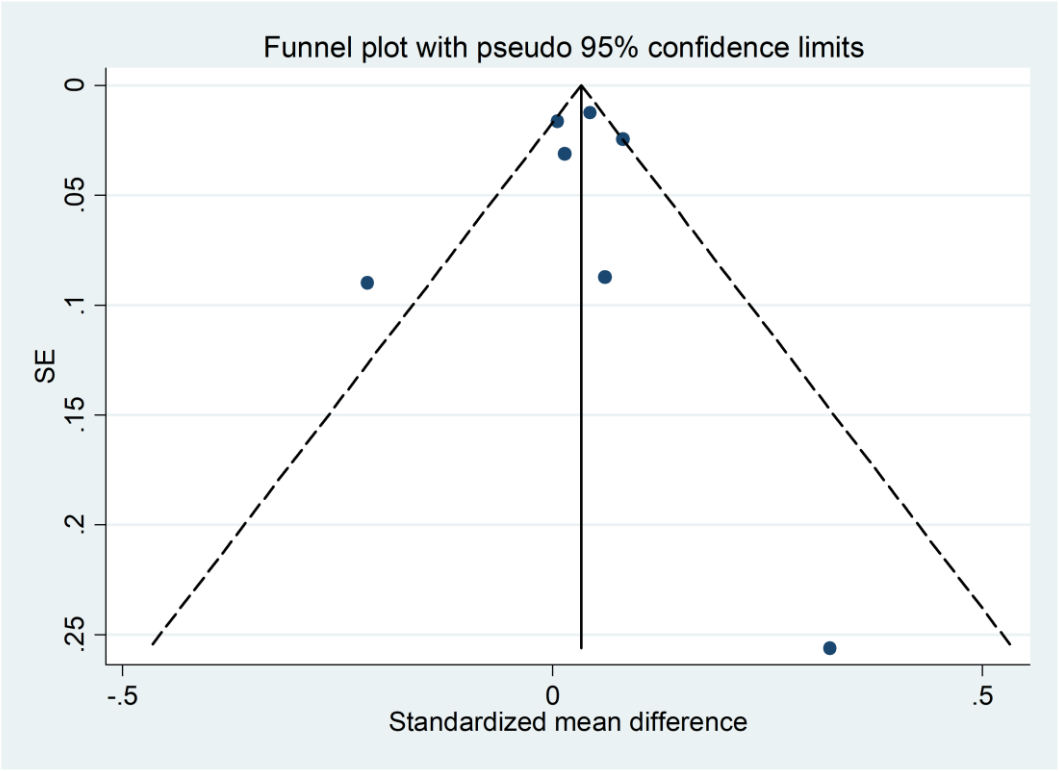
Supplementary Figure 2A: Meta-analysis of studies examining the relationship between the legalisation of cannabis for medical purposes and levels of use in adolescents and young adults (12-25 years, prior to March 2018).



Supplementary Figure 2B: Funnel plot of studies examining the relationship between legalisation of cannabis for medical purposes and levels of use in adolescents and young adults (12-25 years, I^2=98.6%, prior to March 2018).



Supplementary Figure 3A: Meta-analysis of studies examining the relationship between the legalisation of cannabis for recreational purposes and levels of use in adolescents and young adults (12-25 years, prior to March 2018).



Supplementary Figure 3B: Funnel plot of studies examining the relationship between legalisation of cannabis for recreational purposes and levels of use in adolescents and young adults (12-25 years, I^2=45.0%, prior to March 2018).

PRISMA-DTA Checklist

Section/topic	#	PRISMA-DTA Checklist Item	Reported on page #
TITLE / ABSTRACT			
Title	1	Identify the report as a systematic review (+/- meta-analysis) of diagnostic test accuracy (DTA) studies.	1 & 2
Abstract	2	Abstract: See PRISMA-DTA for abstracts.	2-3
INTRODUCTION			
Rationale	3	Describe the rationale for the review in the context of what is already known.	5-6
Clinical role of index test	D1	State the scientific and clinical background, including the intended use and clinical role of the index test, and if applicable, the rationale for minimally acceptable test accuracy (or minimum difference in accuracy for comparative design).	6
Objectives	4	Provide an explicit statement of question(s) being addressed in terms of participants, index test(s), and target condition(s).	6
METHODS			
Protocol and registration	5	Indicate if a review protocol exists, if and where it can be accessed (e.g., Web address), and, if available, provide registration information including registration number.	6-8
Eligibility criteria	6	Specify study characteristics (participants, setting, index test(s), reference standard(s), target condition(s), and study design) and report characteristics (e.g., years considered, language, publication status) used as criteria for eligibility, giving rationale.	7-8
Information sources	7	Describe all information sources (e.g., databases with dates of coverage, contact with study authors to identify additional studies) in the search and date last searched.	6-7
Search	8	Present full search strategies for all electronic databases and other sources searched, including any limits used, such that they could be repeated.	6-7
Study selection	9	State the process for selecting studies (i.e., screening, eligibility, included in systematic review, and, if applicable, included in the meta-analysis).	6-7
Data collection process	10	Describe method of data extraction from reports (e.g., piloted forms, independently, in duplicate) and any processes for obtaining and confirming data from investigators.	8
Definitions for data extraction	11	Provide definitions used in data extraction and classifications of target condition(s), index test(s), reference standard(s) and other characteristics (e.g. study design, clinical setting).	8
Risk of bias and applicability	12	Describe methods used for assessing risk of bias in individual studies and concerns regarding the applicability to the review question.	6-7
Diagnostic accuracy measures	13	State the principal diagnostic accuracy measure(s) reported (e.g. sensitivity, specificity) and state the unit of assessment (e.g. per-patient, per-lesion).	N/A
Synthesis of results	14	Describe methods of handling data, combining results of studies and describing variability between studies. This could include, but is not limited to: a) handling of multiple definitions of target condition. b) handling of multiple thresholds of test positivity, c) handling multiple index test readers, d) handling of indeterminate test results, e) grouping and comparing tests, f) handling of different reference standards	8-9

PRISMA-DTA Checklist

Section/topic	#	PRISMA-DTA Checklist Item	Reported on page #
Meta-analysis	D2	Report the statistical methods used for meta-analyses, if performed.	8-9
Additional analyses	16	Describe methods of additional analyses (e.g., sensitivity or subgroup analyses, meta-regression), if done, indicating which were pre-specified.	8-9
RESULTS			
Study selection	17	Provide numbers of studies screened, assessed for eligibility, included in the review (and included in meta-analysis, if applicable) with reasons for exclusions at each stage, ideally with a flow diagram.	9-10
Study characteristics	18	For each included study provide citations and present key characteristics including: a) participant characteristics (presentation, prior testing), b) clinical setting, c) study design, d) target condition definition, e) index test, f) reference standard, g) sample size, h) funding sources	10-11, Tables 1, 2&3
Risk of bias and applicability	19	Present evaluation of risk of bias and concerns regarding applicability for each study.	11-14
Results of individual studies	20	For each analysis in each study (e.g. unique combination of index test, reference standard, and positivity threshold) report 2x2 data (TP, FP, FN, TN) with estimates of diagnostic accuracy and confidence intervals, ideally with a forest or receiver operator characteristic (ROC) plot.	N/A
Synthesis of results	21	Describe test accuracy, including variability; if meta-analysis was done, include results and confidence intervals.	11-12; 13; 14
Additional analysis	23	Give results of additional analyses, if done (e.g., sensitivity or subgroup analyses, meta-regression; analysis of index test: failure rates, proportion of inconclusive results, adverse events).	11-12; 13; 14
DISCUSSION			
Summary of evidence	24	Summarize the main findings including the strength of evidence.	14-15
Limitations	25	Discuss limitations from included studies (e.g. risk of bias and concerns regarding applicability) and from the review process (e.g. incomplete retrieval of identified research).	15-17
Conclusions	26	Provide a general interpretation of the results in the context of other evidence. Discuss implications for future research and clinical practice (e.g. the intended use and clinical role of the index test).	18-19
FUNDING			
Funding	27	For the systematic review, describe the sources of funding and other support and the role of the funders.	N/A

Adapted From: McInnes MDF, Moher D, Thombs BD, McGrath TA, Bossuyt PM, The PRISMA-DTA Group (2018). Preferred Reporting Items for a Systematic Review and Meta-analysis of Diagnostic Test Accuracy Studies: The PRISMA-DTA Statement. JAMA. 2018 Jan 23;319(4):388-396. doi: 10.1001/jama.2017.19163.

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BMJ Open

Does liberalisation of cannabis policy influence levels of use in adolescents and young adults? A systematic review and meta-analysis

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Primary Subject Heading:	Public health
Secondary Subject Heading:	Addiction
Keywords:	Cannabis, Marijuana, Adolescents, Policy

Does liberalisation of cannabis policy influence levels of use in adolescents and young adults? A systematic review and meta-analysis

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Does liberalisation of cannabis policy influence levels of use in adolescents and young adults? A systematic review and meta-analysis

Keywords : cannabis, marijuana, decriminalisation, legalisation, epidemiology, adolescents, young adults

Abstract

Objectives: To examine the effect of cannabis policy liberalisation (decriminalisation, legalisation) levels of use in adolescents and young adults.

Design: Systematic review and meta-analysis.

Inclusion criteria: Included studies were conducted among individuals younger than 25 years and quantitatively assessing consequences of cannabis policy change. We excluded articles: a) exclusively based on participants older than 25; b) only reporting changes in perceptions of cannabis use; c) not including at least two measures of cannabis use; d) not including quantitative data; e) reviews, letters, opinions and policy papers. Pubmed, PsycINFO, Embase and Web of Science were searched through March 1st 2018.

Data extraction and synthesis: Two independent readers reviewed the eligibility of titles and abstracts, read eligible articles, and four authors assessed the risk of bias (Quality Assessment Tool for Observational Cohort and Cross-Sectional Studies). Extracted data were meta-analysed. The protocol was registered with PROSPERO (CRD42018083950).

Results: 3438 records were identified via search terms and 4 via citation lists; 2312 were retained after removal of duplicates, 99 were assessed for eligibility and 41 were included in our systematic review. 13 articles examined cannabis decriminalisation, 20 legalisation for medical purposes and 8 legalisation for recreational purposes. Findings regarding the consequences of cannabis decriminalisation or legalisation for medical purposes were too heterogeneous to be meta-analysed. Our systematic review and meta-analysis suggest a

small increase in cannabis use among adolescents and young adults following legalisation of cannabis for recreational purposes (standardised mean difference of 0.03, 95% CI -0.01-0.07). Nevertheless, studies characterised by a very low/low risk of bias showed no evidence of changes in cannabis use following policy modifications.

Conclusions: Cannabis policy liberalisation does not appear to result in significant changes in youths' use, with the possible exception of legalisation for recreational purposes which requires monitoring.

Strengths and limitations of this study

- To date, this is the first study to attempt to summarise research on the consequences of various types of changes in cannabis laws and policies (decriminalisation as well as different forms of legalisation) with regard to patterns of use among adolescents and young adults.
- Various data sources in the fields of public health, economics, and public policy were searched in a systematic way.
- The duration of follow-up varied across studies, partly because changes in cannabis policy occurred in different periods and places.
- Among studies examining the consequences of the legalisation of cannabis for recreational purposes, only one was characterised by a very low risk of bias and 5 by a low risk of bias, therefore the findings will need to be confirmed in future research.

Introduction

Cannabis is one of the most frequently used psychoactive substances in North America, Europe, Oceania, and North Africa (12-month prevalence of 3.8% in the world)[1]. Since the 1961 Single Convention on Narcotic Drugs, cannabis is illegal in most countries. However, in the past 20 years a majority of US states (thirty one including the District of Columbia) and several countries (e.g. Spain, Uruguay, Portugal) have liberalised their cannabis legislation by decriminalising or legalising use for medical or recreational purposes[2]. Decriminalisation is the reduction of penalties for cannabis use, while maintaining penalties for cannabis supply. Legalisation is the permission to use and supply oneself (via home growing or controlled sale). Legalisation for medical use is permission to use and sometimes supply with the involvement of a medical professional (e.g. with a doctor's prescription or recommendation)[3].

In many settings - especially where cannabis is widely used – public support for legalisation is widespread[4 5]. For cannabis users, decriminalised or regulated access to the substance decreases the legal and criminal risks incurred. Potential collective benefits of cannabis policy liberalisation include: a) reduced law enforcement costs, b) improvements in the quality of the substance used, c) in case of commercial legalisation, additional tax revenue[6].

Still, cannabis is a source of addiction and can have deleterious health consequences in the short and long-terms, including impairments in memory and concentration[7], risk of injury, or respiratory problems[8]. Moreover, liberalised access to cannabis could also influence the levels of use of other psychoactive substances (e.g. tobacco, alcohol)[9 10]. At the same time, there is also evidence that in the United States, the recent increase in opioid use

is less marked in states which recently implemented policies liberalising cannabis regulations[11].

In adults, the liberalisation of cannabis policy has been followed by increases in levels of heavy cannabis use[12-15]. This may be driven by reductions in the perceived risks[16], price decreases, as well as increases in cannabis availability[13 15]. However, in adolescents, who may be especially vulnerable to the negative consequences of cannabis[7], the impact of policy liberalisation is unclear[13]. As additional US states and European countries are considering liberalising cannabis legislation, there is need to evaluate the potential public health consequences of such policy change.

The objectives of this study were to gain better understanding of the influence of changes in cannabis policy on patterns of use among adolescents and young adults. Youths are a high risk group in terms of illegal substance use and may be especially sensitive to changes in policy; at the same time they may also be especially vulnerable to the biological, psychological and behavioural consequences of cannabis. Data published before March 1st 2018 on this topic were systematically reviewed and meta-analysed.

Methods

Search strategy

Following PRISMA guidelines[17], we conducted a systematic review of studies testing quantitative differences in cannabis use among adolescents and young adults before and after policy change, published prior to March 1, 2018.

Specifically, the following search terms were introduced in Pubmed, Web of Science, EMBASE, PsycINFO: (law* OR decriminalisation OR legalisation) AND (cannabis OR pot OR weed OR marijuana OR grass) AND (young OR youth OR adolescen* OR teen* OR school* OR student). Searches were specified for both MeSH terms and text words and were modified to

meet the requirements of each database. Only articles in English were identified. All titles and abstracts were independently screened by two of the authors to determine potential eligibility. Full texts of all potentially eligible studies were read by two of the authors (FH, MAdS) and discussed with all other authors in case of disagreement. The protocol was registered in PROSPERO (CRD42018083950) and followed the PRISMA framework[17]. The full search strategy is detailed in Supplementary material (Figure 1).

Inclusion criteria

To be included, studies had to be conducted among individuals younger than 25 years and quantitatively assess whether cannabis policy change (defined as decriminalisation, or legalisation of cannabis use for medical or recreational purposes) as compared to no change or the situation prior to change, was associated with changes in cannabis use. This age limit was selected as it is a meaningful cut-off for the potentially negative biological and social effects of cannabis[7] as well as a frequently-used upper bound to define young people. We excluded articles: a) exclusively based on participants older than 25 years; b) only reporting changes in perceptions of cannabis use; c) not including at least two measures of cannabis use and which did not make it possible to compare changes between before and after policy change; d) not including quantitative data; e) reviews, letters, opinions and policy papers.

Patient and public involvement

This research was based on analyses of previously published studies and did not involve direct patient involvement.

Risk of bias

In order to judge the quality of studies that were analysed, risk of bias was assessed using the Quality Assessment Tool for Observational Cohort and Cross-Sectional Studies developed by the National Institute of Health (NIH) (https://www.nhlbi.nih.gov/health-

pro/guidelines/in-develop/cardiovascular-risk-reduction/tools/cohort). Four independent raters evaluated each study (two per article) on up to 11 items including characteristics of the study population, exposure and outcome measurement, time frame adequacy, loss to follow-up (cohort studies; <20% being considered as associated with low bias), adjustment for confounders. Studies defined as presenting a very low risk of bias had no identified flaws. Studies characterised by a low risk of bias provided insufficient information regarding the study time frame or loss to follow-up (where applicable). Studies considered to present a possible risk of bias were characterised by any of the following: a) insufficient information about the study population recruitment or follow-up (where applicable), b) insufficient definition of exposure or outcome, c) a study period of < 1 year between exposure and outcome, or d) insufficient adjustment for potentially confounding individual or contextual factors. Studies considered to present a probable risk of bias were characterised by two or more of the risks identified above. Differences in ratings between coders were discussed in joint meetings.

Data extraction

A coding sheet was developed to identify: study authors, place of study, type of policy change/ study period, participant characteristics (ns), study design, cannabis use measure, statistical methods used/covariates controlled for, key findings and risk of bias.

Meta-analysis

To meta-analyse the effects of the liberalisation of cannabis policy on levels of use, we calculated Standardised Mean Differences (SMD) and associated 95% confidence intervals for each finding using the Practical Meta-Analysis Effect Size Calculator[18]. Effects sizes from different studies were combined into a weighted mean effect size. Each effect size was weighted by the inverse of its variance and then averaged[19]. Standard meta-analytical

procedures suppose the independence of effects[20]. However, several primary studies provided multiple correlated effect size estimates for the same underlying outcome (e.g. 30-day use, 12-month use etc.). To avoid the loss of information resulting from the selection of only one effect size per study, we used the Robust Variance Estimation (RVE) method[21], which makes it possible to handle statistically dependent effect sizes. A fixed effect meta-analysis was undertaken in the absence of significant heterogeneity, otherwise a random effects model was used [22]. To test for homogeneity, we computed the Q statistic to determine whether each set of effect sizes shared a common population effect size[19]. To interpret between-study heterogeneity, we used the I^2 statistic; an I^2 <= 50% is generally considered to indicate low heterogeneity[23].

To study whether cannabis use in adolescents and young adults varied as a function of 1) cannabis decriminalisation, 2) legalisation of cannabis use for medical purposes or 3) legalisation of cannabis use for recreational purposes, we conducted three main meta-analyses.

For each type of cannabis policy change, we also performed a priori hypothesised subgroup analyses, according to study design (cohort vs. cross-sectional), study year (< 2000 vs. ≥ 2000), participants' age (< vs. ≥ 18 years) and the measure of cannabis use (30-day use vs. 12-month use). Studies included in this review did not present stratified results based on whether participants were < vs. ≥ 21 years (the legal age for cannabis use in US states which legalised the substance), making it impossible for us to conduct sensitivity analyses using this age cut-off.

Finally, because the results of a meta-analysis can be biased by studies with non-significant results being less likely to be published, we examined publication bias graphically,

using a funnel plot. All analyses were performed using STATA 14.0 and the *robumeta* macro [24].

Results

The study flowchart (**Figure 1**) shows our search strategy which resulted in the identification of 41 original research reports to be analysed.

The 41 studies analysed were all published in English: 33 were conducted in the United States[25-57], 3 in Australia[58-60], 2 in the United Kingdom[61 62], 1 in the Netherlands[63], 1 in the Czech Republic[64], and 1 internationally[65]. Thirteen studies evaluated the consequences of cannabis decriminalisation[25-28 37 58-65], 20 the consequences of legalisation of use for medical purposes[29-36 38-45 49 53-55], and 8 the consequences of legalisation of use and possession for recreational purposes[46-48 50-52 56 57]. All studies examining the effects of cannabis legalisation (for medical or recreational purposes) were based in the United States.

The reports included were heterogeneous in terms of the populations studied: 21 focused on adolescents (12-17 years)[25 28 31 33-35 38 41-44 46-50 53 55 56 61 65], 6 on young adults (18-25 years)[37 40 52 57 58 60] and 14 included data on both of these groups[14 26 27 29 30 32 36 39 45 51 58 61-63].

Among studies conducted in the United States, 9 were based on the National Study on Drug Use and Health conducted by the Substance Abuse and Mental Health Services Administration (NSDUH https://nsduhweb.rti.org/respweb/homepage.cfm)[14 31 32 36 39 42-45], 7 on the Monitoring The Future study (MTFS http://monitoringthefuture.org/)[25 28 37 38 41 50 54], 4 on the Youth Behavioral Risk Surveillance survey (YBRS https://www.cdc.gov/healthyyouth/data/yrbs/index.htm)[33-35 49] and 4 on the National Longitudinal Study of Youth (NLSY79 https://www.nlsinfo.org/content/cohorts/nlsy79[26 27], and NLSY97 https://www.nlsinfo.org/content/cohorts/nlsy97[33 40].

Among studies conducted in Australia, 2 were based on the National Drug Strategy Household Survey (NDSHS http://data.gov.au/dataset/national-drugs-strategy-household-survey).

Thirty four studies were based on repeated cross-sectional data[25 28 29 31-39 41-45 48-60 62-64], 6 on longitudinal cohort data[26 27 40 46 47 61] and one on analyses of routine administrative data[30]. Sample sizes in individual studies ranged from n=336[30] to > 11,703,100[35].

Overall, 16 studies were characterised by a very low risk of bias[14 31 32 34-36 38 41 44 45 49 50 54 58 59 63] and 9 by a low risk of bias[26 27 30 47 48 51-53 55]; in our systematic review only the results of these investigations were analysed. Given the small number of articles in each category, all studies except those with a high level of bias were meta-analysed. In additional analyses, we verified that findings were stable when studies characterised by probable bias were excluded.

Decriminalisation of cannabis use

As shown in **Table 1**, mong the 13 studies examining the consequences of cannabis decriminalisation, three were characterised by a very low risk of bias[58 59 63]. Two of these - one based in Australia (n=15,468) and the second in the Czech Republic (n=1524), and both conducted among adolescents and young adults, found no evidence of statistically significant changes in patterns of cannabis use following policy change[58 63]. However, one study - based in Australia and conducted exclusively among adolescents aged 12-17 years (n=39,0387) - observed a 12% increase in use following cannabis decriminalisation[59]. We also identified one study characterised by a low risk of bias[26] - conducted in the United States and focusing on 14-21 year olds (n=12,686) - which observed no statistically significant effect of cannabis decriminalisation on youths' use.

Meta-analysing all 13 studies, we observed an I^2 of 99.5%, indicating high heterogeneity. After excluding studies conducted by Williams & Bretteville-Jensen[59] and Miech et al.[37] (Supplementary Figures 1A & 1B), which appeared to be outliers, the I^2 was reduced to 99.1%, but remained too high to conduct a robust meta-analysis. This was unchanged when the analysis was restricted to cohort study data, study year (< or >= 2000), a particular age group (12-17 or 18-25 years), or recent cannabis use (30 days).

Legalisation of cannabis use for medical purposes

As shown in **Table 2**, twenty studies examined the consequences of the legalisation of cannabis use for medical purposes in the United States from 1996 onwards. Twelve were characterised by a very low risk of bias[31 32 34-36 38 41 44 45 49 54]. Of those, six were based on NSDUH data[14 31 32 36 44 45], three on the YRBS[34 35 49] and three on the MTFS[38 41 54]. Altogether six studies (n ranging from 11,453 to 11,703,100) - all conducted among adolescents - one additionally including youths aged 18-20 years[36] and one additionally including youths aged 18-25 years[45] - found no statistically significant effect of the introduction of medical cannabis laws[34-36 38 44 45]. Three of these studies were based on NSDUH data[36 44 45] and two on the YRBS[34 35]. Importantly, both the NSDUH and the YRBS being repeated cross-sectional surveys, the analytical methods used vary across reports in terms of length of follow-up after policy change (from 1 to 9 years), statistical methods (logistic regression[45], difference-in-differences[35], fixed-effects models[36]), as well as covariates. Still, all studies characterised by a very low risk of bias are adjusted for individual demographic characteristics (age, sex, race) as well as contextual factors (at minima a state identifier and the level of cannabis use prior to policy change). In three studies conducted among adolescents, the legalisation of medical cannabis was followed by a decrease in use[32 41 49]. These three reports were based on different large datasets (NSDUH[32], MTFS[41] and YRBS[49], with ns ranging from 11,813 to

973,089). Finally, three studies (ns ranging from 11,813 to 973,089) observed an increase in levels of cannabis use among adolescents (under 18 years) living in a state which passed medical cannabis laws[14 31 54] and one of these observed a similar effect among young adults (ages 18-25 years) [14].

Two studies were characterised by a low risk of bias[30 53]. One, based on routine data (Arrestee Drug Abuse Monitoring system – ADAM, n=336), showed no statistically significant differences in the prevalence of cannabis use (as ascertained by urine tests) among persons seen in hospital emergency departments before and after medical cannabis laws[30]. The second study reported that among cannabis users recruited via social media (n=2,630), the level of cannabis vaping and eating varied with the time since legalisation of medical cannabis – the longer the time since legalisation, the higher the likelihood of use[53].

Importantly, these data indicate that the provisions of laws enabling access to cannabis for medical purposes, such as the amount of cannabis that individuals are allowed to possess and use, the existence of patient registries[49], the proportion of dispensaries per inhabitant, the authorisation of home cultivation, or concomitant laws making it legal to use cannabis for recreational purposes[53] are influential and should be systematically reported by researchers examining the effects of cannabis policies.

Meta-analysing all 20 studies, we observed an I^2 of 100%, indicating high heterogeneity. After excluding the studies conducted by Wen et al.[36] and Harper et al.[32], which appeared to be outliers (Supplementary Figures 2A & 2B), the I^2 was reduced to 98.6%, but remained too high to conduct a robust meta-analysis. This was unchanged when the analysis was restricted to cohort studies, study year (< or >= 2000), a particular age group (12-17 or 18-25 years), or recent cannabis use (30 days).

Legalisation of cannabis for recreational purposes

As shown in **Table 3**, We identified 8 studies examining the impact of recreational cannabis laws, which make it legal to use and possess small amounts of cannabis, on youths. They were all conducted in the United States, where several states have introduced this form of cannabis legalisation since 2012. Four studies were based in Washington state[46 47 48 52], two in Colorado[56 65], one in Washington state and Colorado[50] and one in Oregon[51]. Only one study - based on the MTFS - was characterised by a very low risk of bias[50]. This investigation (n=253,902) reported a statistically significant increase in cannabis use among adolescents living in Washington state (3.2% increase among 8th graders and 5.0% increase among 10th graders), but not among those living in Colorado.

We also identified two studies characterised by a low risk of bias. One (n=13,335) reported a 2.0-3.5% increase in the frequency of cannabis use among college students living in Washington state[52] and the other an increase of .02% among middle and high school students living in Colorado (n=24,171)[65].

Meta-analysing all 8 studies, we observed an I^2 of 89.8%, indicating high heterogeneity (Supplementary Figures 3A & 3B). After excluding the study conducted by Cerda et al.[50], which appeared to be an outlier, the I^2 was reduced to 45.0%. This analysis yielded an average standardised mean difference of 0.03 (95% CI -0.01-0.07), suggesting a possible small increase in the use of cannabis following the legalisation of recreational cannabis.

Discussion

Main findings

Our systematic review of studies examining the impact of the liberalisation of cannabis legislation on patterns of use among adolescents and young people, identified 41 reports published prior to March 2018, 16 characterised by a very low risk of bias and 9 by a low risk of bias. With the exception of one study, high quality reports examining the impact of cannabis decriminalisation (n=4) show no statistically significant change in youths' patterns of use. Similarly, the legalisation of cannabis use for medical purposes, extensively evaluated in the United States, does not appear to have an effect: 6 studies suggest no change in cannabis use among youths, 3 studies observe a decrease, and 4 studies report an increase. However, the legalisation of cannabis for recreational purposes, examined in 6 studies with a very low or low risk of bias, may be associated with a small increase in levels of use among youths.

Overall, policies regarding cannabis use and possession seem to have little effect on actual patterns of use among young people, with the possible exception of the legalisation of recreational use. To date, evidence regarding the impact of the legalisation of recreational cannabis comes from the United States, where prevalence levels of substance use are high and laws liberalising cannabis use tend to be market-oriented. Additional data from other settings (e.g. Uruguay, Canada) will help gain a better understanding of relations between cannabis policy and patterns of use in the population.

Limitations and strengths

Our systematic review and meta-analysis has limitations which need to be acknowledged. First, the specific provisions of laws and policies regulating cannabis and which can influence actual access to the substance[2], vary across settings. For example, decriminalisation can imply different limits on the amount of cannabis that leads to a fine – e.g. the possession of 15 g of herb or 5 g of resin in the Czech Republic is fined approximately

550 euros[63]; in the Australian Capital Territory (Canberra region) the possession of up to 25 g is fined approximately 100 euros, while in Western Australia (Perth region) the possession of less than 10 g is tolerated but higher quantities can result in a conviction[66]. Similarly, laws allowing the use and possession of cannabis for medical purposes, currently in place in approximately 20 countries (e.g. Australia, Belgium, Spain, Canada and some U.S. states) take different forms. For instance, only the Netherlands and some U.S. states make it possible for individuals to purchase or grow cannabis that can be smoked – in other settings individuals can purchase specific medicines derived from cannabinoids (e.g. the United Kingdom). The legal age at which individuals are authorised to possess cannabis (18 or 21 years) varies across settings, with possibly differential effects on levels of use among young adults. Finally, the price of cannabis, which influences levels of use among young people[58 67], varies from place to place and over time. Clearly, differences in specific policy provisions, which have an impact on cannabis availability, make it difficult to compare different settings. Nevertheless, at the time of its implementation or even before if there is wide media coverage, policy change in and of itself can influence the perceptions of cannabis, which in turn shape levels of use[41], justifying the conduct of this systematic review. Second, the duration of follow-up varies across studies, in part because changes in cannabis policy occurred in different periods and places. This is especially a concern for reports evaluating the impact of recreational cannabis laws: policy changes introduced decades ago (e.g. the Netherlands) were not fully evaluated, while follow-up is limited for more recent policy modifications (e.g. the United States, Uruguay). It is unclear whether the introduction of policies that liberalise cannabis use and possession is most likely to influence patterns of use in the short or in the long-term; in the present report we considered that a follow-up period of at least one year following actual policy implementation was necessary to test a possible

effect. Third, among studies examining the consequences of the legalisation of cannabis for recreational purposes, we only identified one study characterised by a very low risk of bias and 5 by a low risk of bias, and the findings we report will need to be confirmed. Our attempt to meta-analyse the results of different studies included in this review proved inconclusive, with the exception of legalisation of cannabis for recreational purposes: this calls for additional, methodologically robust, studies in this area. Fourth, although changes in cannabis policies have occurred in various settings, most studies included in this report were conducted in the United States, where most research in this area has been conducted. It is difficult to assess the extent to which the findings observed in the U.S. will generalise to other countries, and it will be important to update knowledge in this area once data from other places (e.g. Uruguay, Canada) become available.

Despite these limitations, our study has several strengths: a) the evaluation of studies published in different disciplines (public health, epidemiology, economics, social policy) through multiple databases; b) the combination of data from different settings (United States, Australia, Europe); c) special attention to the risk of bias, examined using a framework especially developed for observational studies. Moreover, our systematic review takes into consideration different forms of liberalisation of cannabis policies (decriminalisation, legalisation for medical purposes and for recreational purposes), attempting to tackle this complex issue in a thorough way.

Methodological issues

The studies included in this systematic review relied on several different datasets and applied quite varied methods (logistic regression[45], difference-in-differences[35], fixed-effects models[36]), to isolate the effects of policy change on patterns of cannabis use independently

of individual and contextual characteristics; such triangulation of different methods is considered especially reliable when, as in this case, it yields consistent results[68]. Importantly, because cannabis policy changes most often occur in settings where public support and levels of use are high, it is essential to take into account levels of cannabis use prior to policy change, as was the case in all reports we considered to present a very low or low risk of bias. Finally, it is important to note that we evaluated relative changes in cannabis use post vs. pre policy change. Levels of cannabis use vary widely across settings and in some places may have been so high prior to policy change that additional increases are unlikely (this may be the case of Colorado where over 25% of 12th graders use cannabis on a monthly basis)[50].

Most studies included in our systematic review were cross-sectional, because reports based on longitudinal data are less numerous and were not always of sufficiently high quality. While repeated cross-sectional studies are well-suited to examine long-term changes in patterns of cannabis use in relation to changes in the legal context, additional evidence from longitudinal data following young people would make it possible to take into account individual characteristics and further strengthen the inference that can be drawn regarding the impact of cannabis policy change.

Implications

Summarising the available evidence, we found that, contrary to what has been observed in adults[36 58 69], cannabis decriminalisation and legalisation for medical purposes are probably not related to significant changes in patterns of use among adolescents and young people. This was also recently reported by a systematic review and meta-analysis which focused on medical cannabis laws and patterns of use in the preceding 30 days among adolescents[70]. On the other hand, the legalisation of cannabis use for recreational purposes may lead to higher levels of use in this age group and a younger age at initiation. Several hypotheses have been

proposed to explain this multifactorial phenomenon: a) changes in the reporting of cannabis use; b) a decrease in perceived harmfulness[41]; c) an increase in cannabis availability and access; d) a decrease in price (in legal outlets or on the black market)[71]. While the liberalisation of cannabis policy can have both collective and individual benefits (e.g. decrease in costs of law enforcement, increase in quality control, reduction in individuals' difficulties with the legal system), these data suggest the possibility of small negative public health implications. Adolescents and young adults are especially vulnerable to the consequences of cannabis use, in terms of both biological and social development[72 73], therefore policies that involve the legalisation of recreational use of cannabis need to be accompanied by prevention efforts targeted towards young people. The most effective prevention programs aim to improve school climate and strengthen youths' psychosocial skills such as self-esteem and conflict resolution[74 75].

Conclusion

In recent decades, cannabis policies have been liberalised in different ways (decriminalisation, legalisation of use for medical or recreational purposes) and in various settings. Our systematic review and meta-analysis of 41 research articles published across disciplines (epidemiology, economics, social policy) and using a variety of datasets and statistical methods shows that cannabis decriminalisation or legalisation of use for medical purposes do not result in higher levels of use among youths. Legalisation of use for recreational purposes appears to possibly result in a small increase. It will be important to reassess whether this tendency persists over time, varies across subgroups of youths (male vs. female, urban vs. rural, socioeconomically disadvantaged vs. favoured), and is comparable across settings, particularly as additional countries introduce changes in cannabis policy (e.g. Canada). Repeated cross-sectional as well as longitudinal studies will be

necessary to thoroughly evaluate adolescents' levels of cannabis use following changes in policy.

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Contributors : MM had the original idea for the study and proposed the study design. FH and MAdS conducted the literature search, screened and selected the studies initially identified. MM, CB, MAdS and MMK read and evaluated the quality of the studies included. AN and FEK conducted the meta-analysis. MM wrote the initial manuscript and serves as guarantor. All authors contributed to interpreting the study findings and to the final manuscript.

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Figure legend: Figure 1. Flowchart showing the screening and selection process of articles selected for the study of the impact of liberalisation of cannabis policy with regard to levels of use in adolescents and young adults.

Table 1. Studies examining cannabis use levels in adolescents before and after decriminalisation of cannabis possession (1981-2017).

	Study	Place of study	Type of policy change/study period	Participant characteristics / n	Study design	Cannabis use measures (frequency/ period)	Statistical methods/ covariates	Key findings/effect size	Risk of bias[1] (/10)
1	Johnston et al., 1981[25]	California, Maine, Minnesota, Ohio (early change) + North Carolina, New York, Missouri (late change) vs. states with no decriminalisation	Decriminalisation of cannabis possession in 1975 and 1976	12th grade students participating in the Monitoring the Future surveys (MTFS)/ n~99,000 per year	Cross-sectional survey (1975-1980)	12 months, 30 day, and daily use	Comparisons of prevalence rates	12-month use: d=0.06, 95% CI 0.0003; 0.127; 30-day use: d=0.125, 95% CI 0.059; 0.191(unadjusted)	R1: 8 R2: 8.1 Average: 8.1 Possible
2	Thies & Register, 1993[26]	Alaska, California, Colorado, Maine, Minnesota, Missouri, Nebraska, New York, North Carolina, Ohio, Oregon	Decriminalisation of cannabis possession 1976-1979	14-21 year olds participating in the National Longitudinal Survey of Youths1979 (NLSY) /n=12,686	Cohort study with follow-up in 1984 and 1988.	30 day use	OLS regression models controlled for sex, race, parental education, own education, income, church attendance, marital status, urban setting; legal context regarding underage drinking	1984: d=0.05, 95% CI -0.02; 0.14; 1988: d=0.06, 95% CI -0.03; 0.16 (unadjusted)	R1: 9 R2: 9 Average: 9 Low
3	McGeorge & Aitken, 1997[58]	Australian Capital Territory vs. Melbourne	Decriminalisation of cannabis possession, use and cultivation in 1992	3rd year university students at Australian National University and Melbourne University /n=903	Cross-sectional survey (1994)	12-month use	Chi-square statistics	d=0.21, 95% -0.02; 0.45 (unadjusted)	R1: 6.4 R2: 4.5 Average: 5.5 Probable
4	MacCoun, 1997[63]	Netherlands	Decriminalisation of cannabis in	16-18 year olds participating in a	Repeated cross-sectional	Lifetime use	Comparison of prevalence rates	Netherlands vs. US: d=-0.23; 95% CI -0.26; -	R1: 8.1 R2: 8.2

[1] R1 : Rater 1 ; R2 : Rater 2

			1976 followed by legalisation in 1984	school-based survey (Trimbos) vs. Youths of the same age in the US (Monitoring the Future)/ n~115,000	surveys: 1970 to 1996			0.19 (unadjusted)	Average: 8.2 Possible
5	Pacula 1998[27]	Alaska, California, Colorado, Maine, Minnesota, Missouri, Nebraska, New York, North Carolina, Ohio, Oregon	Decriminalisation of cannabis possession 1976-1979	14-21 year olds participating in the National Longitudinal Survey of Youths1979 (NLSY)/n=8,008	Cohort study with follow-up in 1984.	30 day use	Two part model controlled for sex, age, race, number of siblings, urban setting, academic achievement, expected years of schooling, illegal activity; parents' marital status, employment status, alcohol use; legal context regarding alcohol use, crime level, beer and cigarette taxes	d=0.0179, 95% CI -0.038; 0.0008	R1: 10.0 R2: 8.1 Average: 9.1 Low
5	DiNardo & Lemieux 2001[28]	California, Colorado, Maine, Minnesota, Mississippi, Nebraska, New York, North Carolina, Ohio, Oregon	Decriminalisation of cannabis possession 1976-1979	12th grade students participating in the Monitoring the Future surveys (MTF) /n~165,000	Cross-sectional survey (1980-1989)	30 day use	Structural regression model controlled for sex, age, race, parental education, weekly hours of work, income, alcohol use, state-level unemployment and alcohol drinking age	d=-0.08, 95% CI -0.12; -0.05	R1: 7.7 R2: 7.7 Average: 7.7 Possible
7	Williams 2004[59]	Australian Capital Territory, Northern Territory vs. non decriminalising states	Decriminalisation of cannabis possession, use and cultivation between 1988 and 1998	14-25 years , Australian National Drug Strategy Household Survey (NDSHS)	Repeated cross-sectional surveys (1988, 1991, 1993, 1995, 1998)	12-month use	Ordered probit model controlled for sex, age, marital status, dependent children, ethnicity, educational level,	d=0.04, 95% CI -0.102; 0.192	R1: 9.2 R2: 10 Average: 9.6 Very low

				/n=15,468			employment, capital city residence, decriminalisation regime		
8	Williams & Bretteville-Jensen, 2014[60]	South Australia, Australian Capital Territory, Northern Territory, Western Australia vs. non-decriminalising states	Decriminalisation of cannabis possession, use and cultivation between 1987 and 2004.	20-40 year old lifetime users of cannabis participating in the Australian National Drug Strategy Household Survey (NDSHS) /n=39,087	Repeated cross-sectional surveys (1998, 2001, 2004, 2007, 2010)	Age at initiation	Difference-in-differences with discrete time hazard model controlled for sex, education, ethnicity, capital city residence, survey year	12-17 years: d=0.57, 95% CI 0.52; 0.63	R1: 10 R2: 10 Average: 10 Very low
9	Fuller, 2014[61]	England	Declassification of cannabis from schedule B to schedule C drug (2004) and then back (2009)	11-15 year olds participating in a representative school survey/n=6,173	Repeated cross-sectional surveys (2001-2014)	12-month use	Prevalence rates	2004 vs. 2009: d=-0.22, 95% CI -0.29; -0.165 (unadjusted)	R1: 6.4 R2: 6.4 Average: 6.4 Probable
10	Braakmann & Jones, 2014[62]	United Kingdom	Declassification of cannabis from schedule B to schedule C drug (2004)	15-25 year olds participating in the Offending, Crime and Justice Survey (OCJS)/n=2,539	Cohort study (2003-2006)	12-month and 30-day use;	Difference-in-differences model controlled for age and calendar year	12-month use; 15-17 yrs: d=-0.01, 95% CI -0.07; 0.002; 18-25 yrs: d=-0.05, 95% CI -0.15; 0.05; 30-day use: 15-17 years: -0.006, 95% CI -0.009; 0.08; 18-20 years: -0.13, 95% CI -0.24; -0.02	R1: 8.6 R2: 8.0 Average: 8.3 Possible
11	Miech et al, 2015[37]	California vs. other US states	Decriminalisation in 2010	8th, 10th and 12th grade students participating in the Monitoring the Future surveys (MTF)/n=97,238	Repeated cross-sectional surveys (2007-2012)	12-month and 30-day use	GEE regression models	12-month: d=0.32, 95% CI 0.31-0.34; 30-day use: d=0.57, 95% CI 0.55-0.59 (unadjusted)	R1: 8.6 R2: 9.0 Average: 8.8 Possible
12	Shi et al, 2015[65]	Cross-national study of 38 countries	Depenalisation, decriminalisation, and partial	15 year olds participating in the Health	Repeated cross-sectional surveys	12-month and regular (>=40 times in	Multilevel logistic random intercept regression	12-month use: d=-0.004, 95% CI -0.02; 0.13; regular use:	R1: 8.2 R2: 8.0 Average:

			prohibition changed since 0-5 years, 5-10 years or >10 years	Behaviour in School-Aged Children Study (HBSC)/ n=172,894	(2001/2002, 2005/2006, 2009/2010)	lifetime) use		d=0.17, 95% CI 0.13; 0.20	8.1 Possible
13	Červený J et al, 2017[64]	The Czech Republic	Decriminalisation of cannabis possession in 2010	15-25 years participating in drug use monitoring surveys/ n=1086 in 2008 and 438 in 2012	Repeated cross-sectional surveys (2008-2012)	Age at initiation	Mixed proportional hazards controlled for sex, education, birth cohort and region of residence	d=-0.26, 95% CI -0.37; -0.15 (unadjusted)	R1: 10 R2: 10 Average: 10 Very low

Table 2. Studies examining cannabis use levels in adolescents before and after the legalisation of cannabis use for medical purposes (1996-2018).

	Study	Place of study	Type of policy change/study period	Participant characteristics / n	Study design	Cannabis use measure (frequency/ period)	Statistical methods/ covariates	Key findings/effect size	Risk of bias (/10)[1]
1	Khatapoush & Hallfors, 2004[29]	California (CA)	State-level Medical marijuana laws (MML): Proposition 215 (1996)	16-25 year olds participating in the Robert Wood Johnson Foundation's Fighting Back initiative (FB)/n=2,651	Repeated cross-sectional surveys in 1995, 1997 and 1999.	12-month and 30-day use	Logistic regression model	12-month use: d=0.54, 95% CI 0.48; 0.59; 30-month use: d=0.72, 95% CI 0.64; 0.79 (unadjusted)	R1: 8.6 R2: 8.0 Average: 8.3 Probable
2	Gorman et al, 2007[30]	Los Angeles, San Diego, San Jose (CA), Portland (OR)	State-level Medical marijuana laws (MML) introduced before 2002	10-18 year olds registered in the Arrestee Drug Abuse Monitoring system (ADAM)/ on average n=255 in California & n=81 in Oregon	Routine data collection (1995-2002)	Urine test data (>=50 ng of THC per decilitre)	Interrupted time series design	California: 10-18 yrs: d=-0.42, 95% CI -0.60; -0.24; Oregon: 10-18 yrs: d=-0.75, 95% CI -1.33; -0.17 (unadjusted)	R1: 9.2 R2: 9.1 Average: 9.2 Low
3	Wall et al, 2011[31]	Alaska, California, Colorado, Hawaii, Maine, Nevada, Oregon, Washington + Michigan, Montana, New Mexico, Rhode Island, Vermont + Arizona, Delaware, New Jersey vs. other US states	State-level Medical marijuana laws (MML) introduced before 2002	12-17 olds participating in the National Survey of Drug Use and Health (NSDUH)/ n~11,813	Repeated cross-sectional surveys (2002-2008)	30-day use	Fixed effects model with random intercept, controlled for cannabis use 2002-2008	2002-2003: d=0.15, 95% CI 0.07; 0.23	R1: 9.7 R2: 9.4 Average: 9.6 Very low

[1]R1 : Rater 1 ; R2 : Rater 2

4	Harper et al, 2012[32]	Alaska, California, Colorado, Hawaii, Maine, Nevada, Oregon, Washington + Michigan, Montana, New Mexico, Rhode Island, Vermont vs. other US states	State-level Medical marijuana laws (MML) introduced before 2002	12-17 year olds and 18-25 year olds participating in the National Survey of Drug Use and Health (NSDUH) /n~11,813 per age group	Repeated cross-sectional surveys (2002-2009)	30-day use	Difference-in-differences estimates controlled for measurement error	12-17 years: d=-1.25, 95% CI –1.29; -1.21; 18-25 years: d=1.71, 95% CI 1.67 - 1.75	R1: 9.4 R2: 9.5 Average: 9.5 Very low
5	Anderson et al, 2012[33]	Alaska, Arizona, California, Colorado, Delaware, District of Columbia, Hawaii, Maine, Michigan, Montana, Nevada, New Jersey, New Mexico, Oregon, Rhode Island, Vermont, Washington vs. other US states	State-level Medical marijuana laws (MML) introduced before 2011	15-19 years olds participating in the National and State Youth Risk Behavior Surveys (YRBS) /n=786,568	Repeated cross-sectional surveys (1993-2011)	30-day use; 30-day frequent use;	Linear regression controlled for age, sex, race, grade, state-level marijuana decriminalisation, BAC 0.08 laws, state beer tax, income per capita, unemployment	YRBS: 30day use: d=-0.32, 95% CI -0.33; -0.32; 30-day frequent use d=-0.18, 95% CI -0.19; -0.18	R1: 8.5 R2: 8.1 Average: 8.3 Possible
6	Lynne-Landsman et al, 2013[34]	Delaware, Michigan, Montana, Rhode Island compared pre and post-MML implementation	State-level Medical marijuana laws (MML) introduced 2003-2009	9-12th graders participating in the Youth Risk Behavior Surveys (YRBS) /n~11,453	Repeated cross-sectional surveys (2003-2009)	30-day use;	Difference in differences controlled for age, ethnicity, and sex	d=0.24, 95% CI 0.20;0.28	R1: 9.2 R2: 10 Average: 9.6 Very low
7	Choo et al, 2014[35]	Idaho vs. Montana, Massachusetts vs. Rhode Island, New Hampshire vs. Maine, Utah vs. Nevada, New York vs. Vermont	State-level Medical marijuana laws (MML)	9-12th graders participating in the Youth Risk Behavior Surveys (YRBS)/ n~11,703,100	Repeated cross-sectional surveys since 1991, 1993, 1995, 1997, 1999, 2001, 2003, 2005, 2007	30 day use	Difference-in-differences controlled for state, year, age, sex, race, grade	d=0.065, 95% CI 0.026; 0.105	R1: 10 R2: 9.5 Average: 9.8 Very low
8	Wen et al, 2014[36]	District of Columbia,	State-level Medical	12-20 year olds participating in	Repeated cross-sectional	30-day use;	Fixed-effects models controlled	d=-1.72, 95% CI:-1.73;-1.71	R1: 9.6 R2: 10

		Michigan, Montana, New Jersey, New Mexico, Rhode Island, Vermont vs US states with no MML laws by 2010	marijuana laws (MML) introduced between 2004 and 2010	the National Survey on Drug Use and Health (NSDUH)/ n~183,600	surveys (2004-2011)		for age, sex, race, self-reported health, cigarette use, urban residence, family poverty, state-level unemployment, mean income, median income, alcohol excise taxes.		Average: 9.8 Very low
9	Hasin et al, 2015[38]	21 US states that passed MML vs. non-MML US states	State-level Medical marijuana laws (MML) introduced by 2014	8th, 10th and 12th grade (13, 15, 17) students participating in the Monitoring the Future surveys (MTF) /n=1,098,070	Repeated cross-sectional surveys (1991-2014)	30-day use;	Multilevel regression models controlled for sex, age, race, parental education, class size, private school, urban setting, state-level proportion of males, whites, persons with no high school education and aged 11-24 years	d=-0.033, 95% CI -0.039; -0.026	R1: 10 R2: 10 Average: 10 Very low
10	Schuermeyer et al, 2015[39]	Colorado vs. 34 non-MML US states	State-level Medical marijuana laws (MML) introduced in 2009	12-20 year olds participating in the National Survey on Drug Use and Health (NSDUH)/ n~158,600 12-17 year olds + 159,200 18-25 year olds	Repeated cross-sectional surveys (2006-2011)	>=20 times in 30-days use	Logistic regression controlled for state, year, age, sex, race, educational level and state-by-year interaction	12-17 yrs: d=0.09, 95% CI -0.04 ; 0.23; 18-25 yrs: 0.23, 95% CI 0.16-0.29 (unadjusted)	R1: 9 R2: 8.2 Average: 8.6 Possible
11	Pacula et al, 2015[40]	Alaska, Arizona, California, Colorado, Delaware, District of Columbia,	State-level Medical marijuana laws (MML) introduced before	- <21 year olds participating in the National Longitudinal Survey of	Cohort study (1997-2011)	30-day use;	Difference-in-differences models controlled for population unemployment	d=-0.0109, 95% CI, -0.03; 0.009	R1: 8.2 R2: 8.6 Average: 8.4 Possible

		Hawaii, Maine, Maryland, Michigan, Montana, Nevada, New Jersey, New Mexico, Oregon, Rhode Island, Vermont, Washington vs. US states with no MML in 2012	2012; comparison of different legal provisions: patient registry; home cultivation; legal dispensaries;	Youths1997 (NLSY)/46,375			rate, age distribution, state beer tax rate, BAC 0.08 tax;		
12	Keyes et al, 2016[41]	21 US states that passed MML vs. non-MML US states	State-level Medical marijuana laws (MML) introduced by 2014	8th, 10th and 12th grade (13, 15, 17) students participating in the Monitoring the Future surveys (MTF) /n=973,089	Repeated cross-sectional surveys (1991-2014)	30-day use;	Time-varying multilevel regression models controlled for sex, age, race, parental education, class size, private school, urban setting, state-level proportion of males, whites, persons with no high school education and aged 11-24 years	d=-0.03, 95% CI -0.03;-0.027	R1: 9.6 R2: 9.5 Average: 9.6 Very low
13	Maxwell & Mendelson, 2016[42]	California, Colorado and Washington vs. other US States	State-level Medical marijuana laws (MML) and Recreational marijuana laws (RML)	12-25 year olds participating in the National Survey of Drug Use and Health (NSDUH)	Repeated cross-sectional surveys (2002-2013)	12-month use	Comparison of prevalence rates	Impossible to calculate	R1: 5 R2: 6.8 Average: 5.9 Probable
14	Stolzenberg et al, 2016[43]	Alaska, Arizona, California, Colorado, Delaware, Hawaii, Maine, Michigan, Montana, Nevada,	State-level Medical marijuana laws (MML) introduced between 1998 and 2011	12-17 olds participating in the National Survey of Drug Use and Health (NSDUH) /n~112,500	Repeated cross-sectional surveys (2002-2011)	30-day use	Random effects model controlled for state-level medical cannabis possession limit, cannabis availability, %	d=0.060, 95% CI 0.034;0.087	R1: 7.3 R2: 8.1 Average: 7.7 Possible

		New Jersey, New Mexico, Oregon, Rhode Island, Vermont, Washington vs. other US states					enrolled in drug class, alcohol use, prior crime conviction, % families on income assistance, % juveniles who skipped school, % families where the father resides in household, % male, % white		
15	Wall et al, 2016[44]	Arizona, Delaware, Michigan, Montana, New Jersey, New Mexico, Rhode Island, Vermont vs. other US states	State-level Medical marijuana laws (MML) introduced between 2004 and 2011	12-17 olds participating in the National Survey of Drug Use and Health (NSDUH) /n~112,500	Repeated cross-sectional surveys (2002-2011)	30-day use	Fixed effects model	d=-0.0059, 95% CI -0.030;0.018	R1: 9.4 R2: 10 Average: 9.7 Very low
16	Martins SS et al, 2016[45]	Arizona, Connecticut, Delaware, Illinois, Massachusetts, Michigan, New Hampshire, New Jersey, New Mexico, Rhode Island vs. other US states	State-level Medical marijuana laws (MML) introduced between 2005 and 2013	12-17 and 18-25 year olds participating in the National Survey of Drug Use and Health (NSDUH)/ n=175,000 12-17 year olds and 175,000 18-25 year-olds	Repeated cross-sectional surveys (2004-2013)	30-day use	Multilevel logistic regression controlled for sex, ethnicity, insurance status, household income, population density, state proportions of sex, ethnicity, youths, education, unemployment, median household income	12-17 yrs: d=0.02, 95% CI -0.04-0.08; 18-25 yrs: d=0.006, 95% CI -0.035 ; 0.047).	R1: 9.1 R2: 10 Average: 9.6 Very low
17	Johnson et al, 2017[49]	Alaska, Arizona, Colorado, Delaware, Maine, Michigan, Montana, Nevada, New Jersey, New Mexico, Rhode Island, Vermont vs.	State-level Medical marijuana laws (MML) introduced between 1998 and 2011	9-12th graders (14-17) participating in the Youth Risk Behavior Surveys (YRBS) /n=715,014	Repeated cross-sectional surveys (1991-2011)	30-day use and 30-day heavy use (>=20 times)	Fixed effect multiple logistic regression controlled for year, state, age, sex, ethnicity	30-day use: d=-0.042, 95% CI -0.051;-0.032; 30-day heavy use: d=0.0001, 95% CI -0.018;0.0185	R1: 9.5 R2: 9.5 Average: 9.5 Very low

		other US states							
18	Borodovsky et al, 2017[53]	Alaska, Colorado, District of Columbia, Oregon, Washington vs. 20 US states that did not	Legalisation status: MML or RCCL vs. no legal cannabis law	14-18 year olds recruited online (via targeted Facebook invitations) /n=2,630	Cross-sectional survey (April 29-May 18, 2016)	30-day cannabis use via smoking, vaporizing, or eating.	Logistic and linear regression controlled for age, gender, race, grade level, lifetime days of cannabis use, age of onset.	d=0.064, 95% CI -0.048;0.176	R1: 9.5 R2: 9.1 Average: 9.3 Low
19	Mauro et al, 2017[14]	Arizona, Connecticut, Delaware, Illinois, Maine, Michigan, New Hampshire, New Jersey, New Mexico, Rhode Island, vs. 27 US states with no MML by 2013	State-level Medical marijuana laws (MML) introduced prior to 2015	12-17 and 18-25 year olds participating in the National Survey of Drug Use and Health (NSDUH) /n~175,000 12-17 year-olds and 175,000 18-25 year year olds	Repeated cross-sectional surveys (2004-2013)	State-level 30-day and daily use	Multilevel linear regression controlled for trends in marijuana use and state-level % males, % White, % aged 10-24 years, % > 25 yrs with no high school degree, % unemployed, median household income.	30-day use: 12-17 years: d=0.041, 95% CI 0.022; 0.059; 18-25 years: d=0.016, 95% CI 0.003; 0.029; daily use: 12-17 years: d=-0.003, 95% CI -0.021; 0.014; 18-25 years: d=0.064, 95% CI 0.050; 0.078	R1: 10 R2: 9.5 Average: 9.8 Very low
20	Cerda et al, 2018[10]	Arizona, California, Colorado, Connecticut, Delaware, Illinois, Maine, Maryland, Massachusetts, Michigan, Minnesota, Montana, Nevada, New Hampshire, New Jersey, New Mexico, New York, Oregon, Rhode Island, Vermont, Washington vs. other US states	State-level Medical marijuana laws (MML) introduced prior to 2015; time since legalisation.	8th, 10th and 12th graders (13, 15, 17) participating in the Monitoring the Future Survey/ n=1,140,768	Repeated cross-sectional survey (1991-2015)	30-day use	Difference-in-differences models controlled for individual grade, age, sex, race/ethnicity, socioeconomic status, number of students per grade, public vs. private school, school in metropolitan statistical area, state-level % males, % White, % aged 10-24 years, and % older than 25 with no high school degree.	d=0.0176, 95% CI 0.0170;0.0182	R1: 10 R2: 10 Average: 10 Very low

Table 3. Studies examining cannabis use levels in adolescents before and after legalisation of recreational cannabis use (2016-2018).

	Study	Place of study	Type of policy change/study period	Participant characteristics / n	Study design	Cannabis use measure (frequency/ period)	Statistical methods/ covariates	Key findings	Risk of bias (/10)[1]
1	Estoup et al, 2016[46]	Washington	Legalisation in 2012	High school students (14-17) with problematic substance use enrolled in high school in the Seattle area/ n=262	Cohort study (2010-2015)	3-month use	Mediation model	d=0.061, 95% CI -0.110; 0.232 (unadjusted)	R1: 7.1 R2: 7.4 Average: 7.3 Possible
2	Mason et al, 2016[47]	Washington vs. other US states	Legalisation in 2012	8th graders (14) in Tacoma, WA participating in a longitudinal study/n=238	Cohort study (2010/2011-2012/2013)	30-day use	Multilevel regression models controlled for substance use initiation prior to baseline	d=0.323, 95% CI -0.177; 0.825	R1: 9.2 R2: 9.1 Average: 9.2 Low
3	Fleming et al, 2016[48]	Washington vs. other US states	Legalisation in 2012	10th (16) graders participating in the biennial Washington state school survey/n=30,365	Repeated cross-sectional surveys (2000-2014)	30-day use	Logistic regression analyses controlled for perceived harm of marijuana, alcohol use, and year	d=0.044, 95% CI -0.019; 0.069	R1: 9.2 R2: 9.2 Average: 9.2 Low
4	Cerdá et al, 2017[50]	Colorado and Washington vs. other US states	Legalisation in 2012	13-18 years participating in the Monitoring the Future surveys (MTF)/ n= 253,902	Repeated cross-sectional surveys (2010-2015)	30-day use	Difference-in-differences	d=1.03, 95% CI 1.00; 1.06	R1: 9.1 R2: 10 Average: 9.6 Very low
5	Kerr et al, 2017[51]	2 universities in Oregon vs. 6 in	Legalisation in 2015	18-26 year old college	Repeated cross-sectional	30-day use	Mixed-effects logistic regression	d=0.0139, 95% CI 0.048; 0.075	R1: 9.5 R2: 8.5

[1] R1 : Rater 1; R2 : Rater 2

		other US states		undergraduates participating in the Healthy Minds Study/n=10,924	surveys (2014 and 2016)		controlled for cigarette use, year in college, age, sex, race, residential type, relationship status, sexual orientation, international student status, depression, anxiety, adjustment, institution size and survey period		Average: 9 Low
6	Miller et al, 2017[52]	Washington	Legalisation in 2012; Opening of licensed retail stores for marijuana in 2014	College students participating in the National College Health Assessment (WSU NCHA)/n=13,335	Repeated cross-sectional surveys (2005, 2006, 2008, 2010, 2012, 2014, 2015)	30-day use	Logistic regression controlled for age, sex, race, year in school, estimated secular increase in cannabis use.	Post MML (2014): d=0.04, 95% CI 0.002 ; 0.083; post-RML (2015): d=0.082, 95% CI 0.034 ; 0.130	R1: 9.5 R2: 8.5 Average: 9 Low
7	Harpin et al, 2018[66]	Colorado	Legalisation in 2012	6-12th grade (11-17) students (Healthy Kids Colorado Survey)/n=24,171	Repeated cross-sectional survey (2013 and 2014)	30-day use	Comparison of prevalence rates	d=0.006, 95% CI -0.026; 0.038 (unadjusted)	R1: 9.4 R2: 9.4 Low
8	Jones et al., 2018[57]	Colorado	Legalisation in 2012	College students(22-24 years) n=1,413	Repeated cross-sectional survey (October 2013, March 2014, October 2014 and March 2015)	Lifetime	Comparison of prevalence rates	d=-0.215, 95% CI -0.385; -0.039 (unadjusted)	R1: 4.4 R2: 5.0 Average: 4.7 High

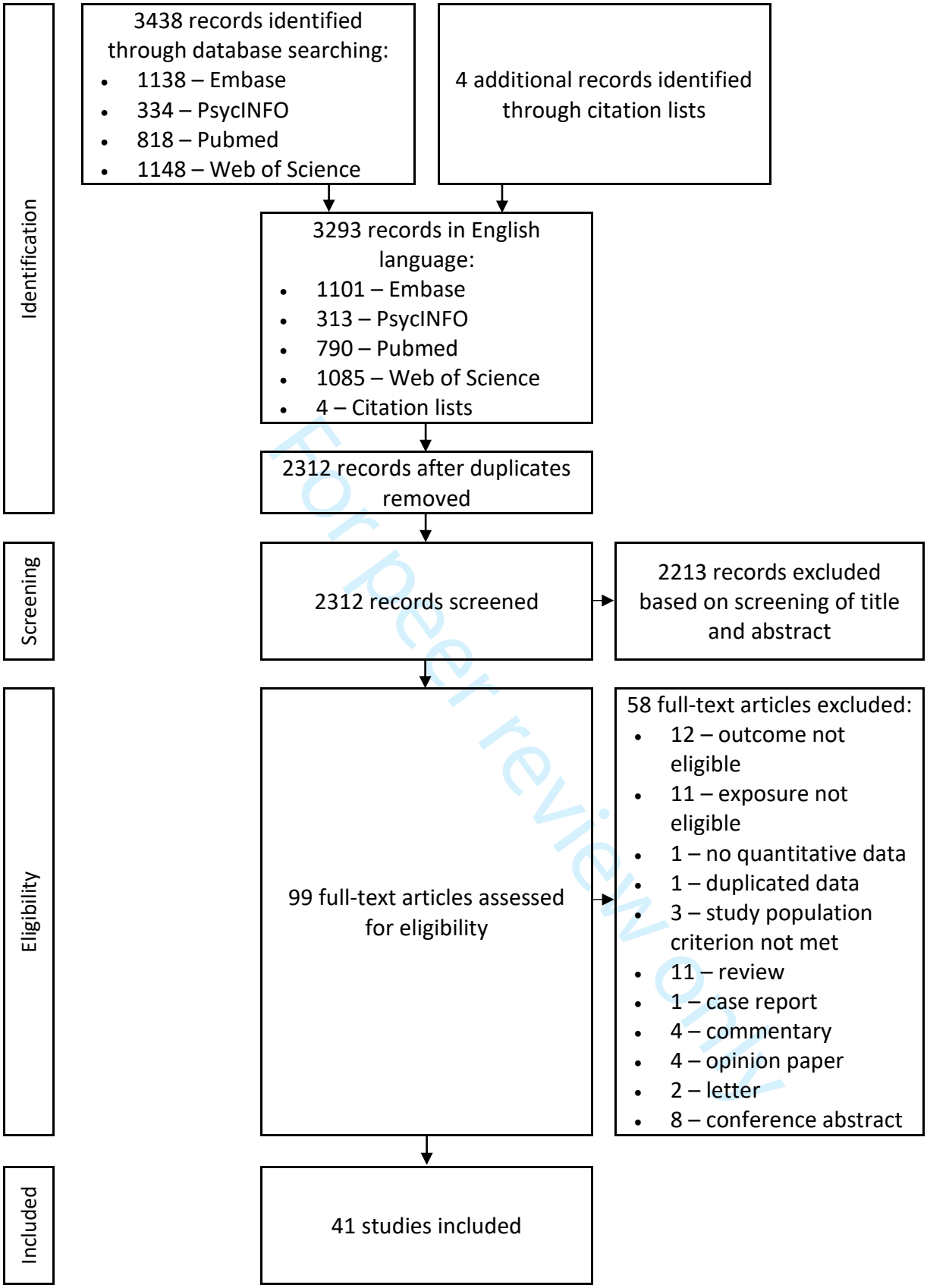


Figure 1. Flowchart showing the screening and selection process of articles selected for the study of the impact of liberalisation of cannabis policy with regard to levels of use in adolescents and young adults.

Supplementary file 1. Full search strategy

Platform: Pubmed

Notes:

1- [MH] indicates MesH Terms
2- [TW] indicates Text Word. Terms that are qualified with this field tag were searched in the following fields: title, abstract, MeSH headings and subheadings, other terms field (which includes author-supplied keywords), secondary source identifier
3- Terms qualified with * were searched with their variations (for different endings)

Search string:

(law*[MH] OR law*[TW] OR decriminalization[MH] OR decriminalization[TW] OR legalization[MH] OR legalization[TW])

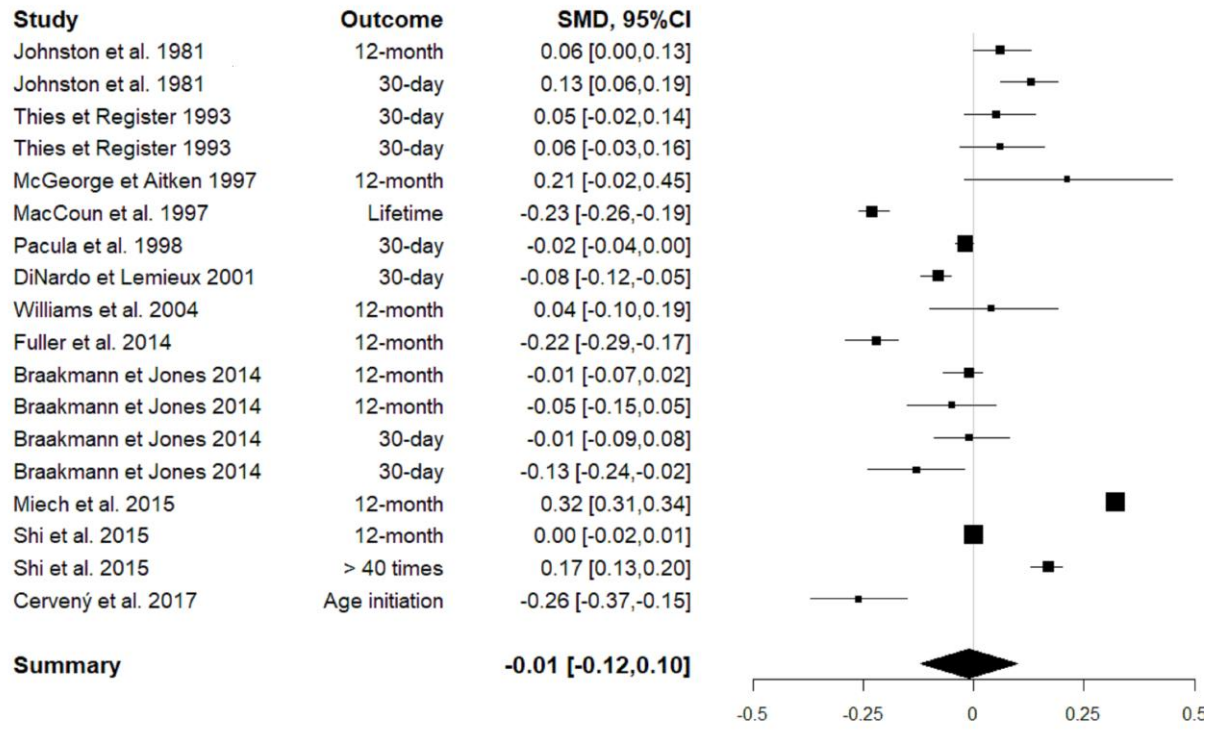
AND

(cannabis[MH] OR cannabis[TW] OR pot[MH] OR pot[TW] OR weed[MH] OR weed[TW] OR marijuana[MH] OR marijuana[TW] OR grass[MH] OR grass[TW])

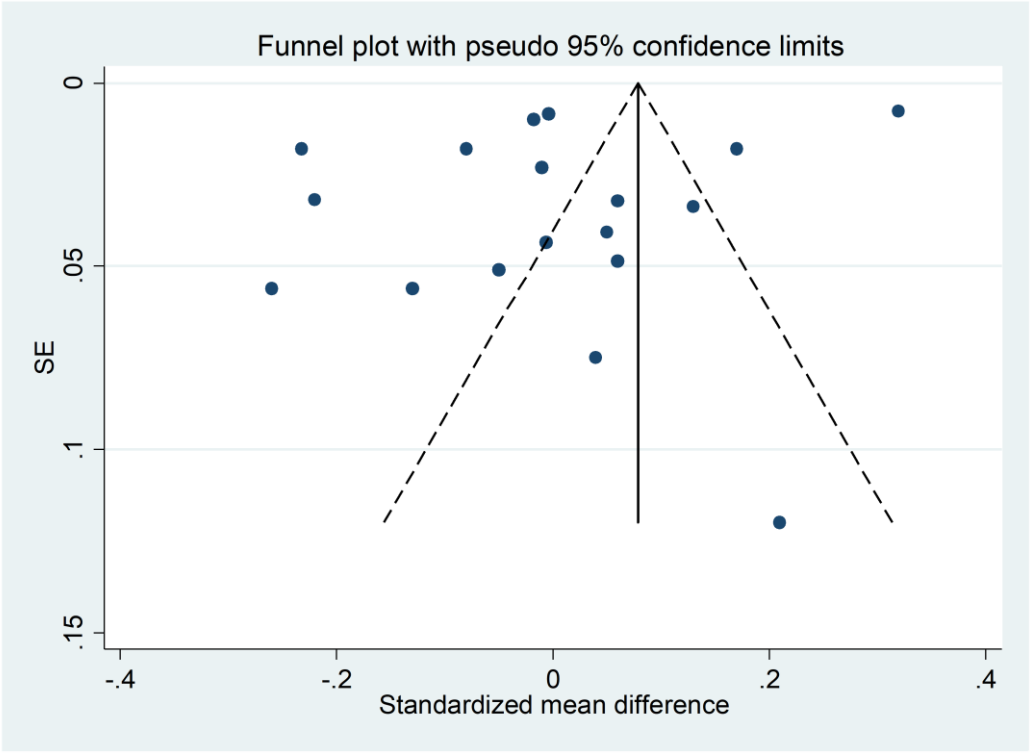
AND

(young[MH] OR young[TW] OR youth[MH] OR youth[TW] OR adolescen*[MH] OR adolescen*[TW] OR teen*[MH] OR teen*[TW] OR school*[MH] OR school*[TW] OR student[MH] OR student[TW])

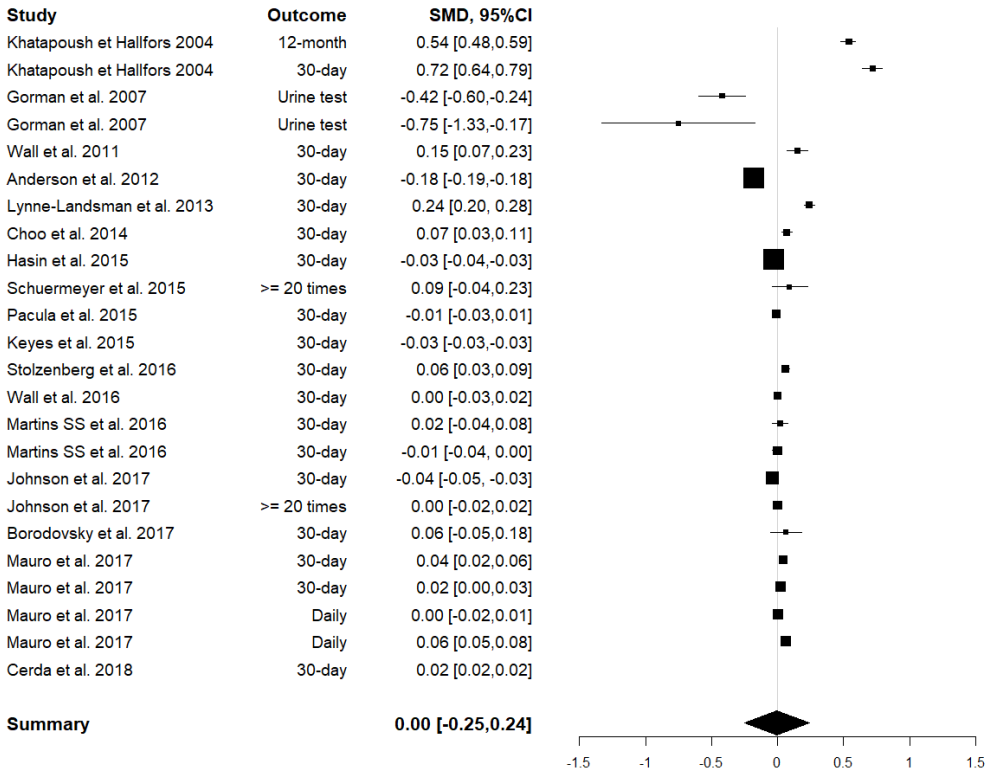
Limits: English language



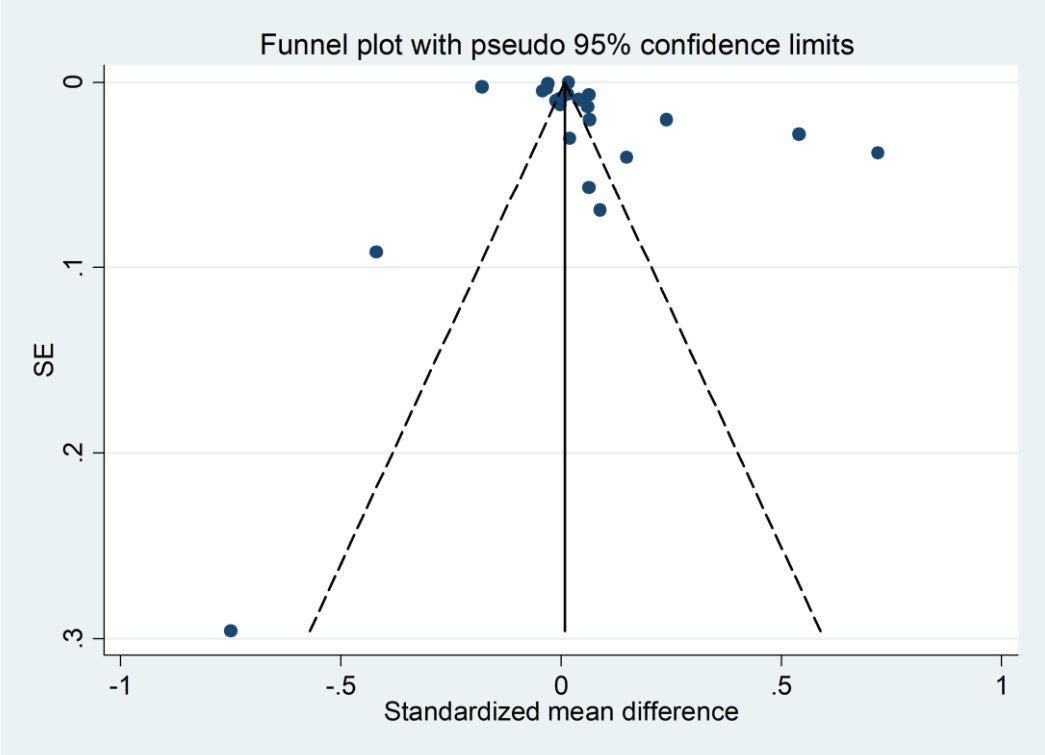
Supplementary Figure 1A: Meta-analysis of studies examining the relationship between cannabis decriminalization and levels of use in adolescents and young adults (12-25 years, prior to March 2018).



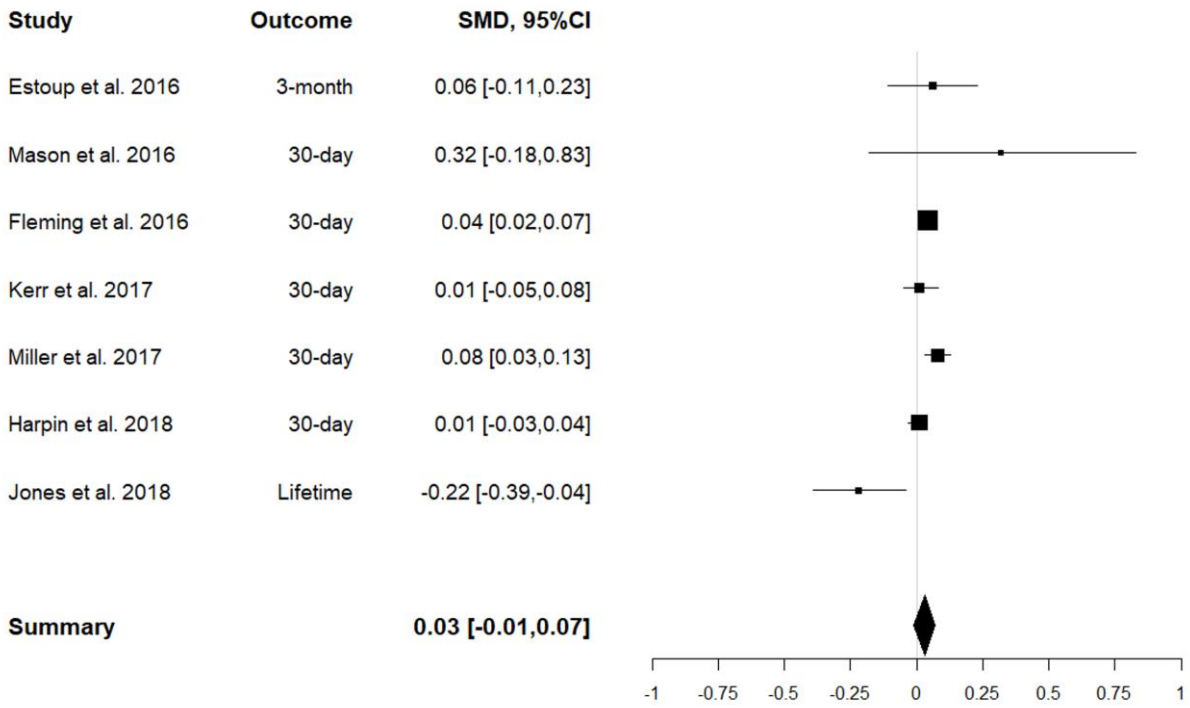
Supplementary Figure 1B: Funnel plot of studies examining the relationship between cannabis decriminalisation and levels of use in adolescents and young adults (12-25 years, I^2=99.1%, prior to March 2018).



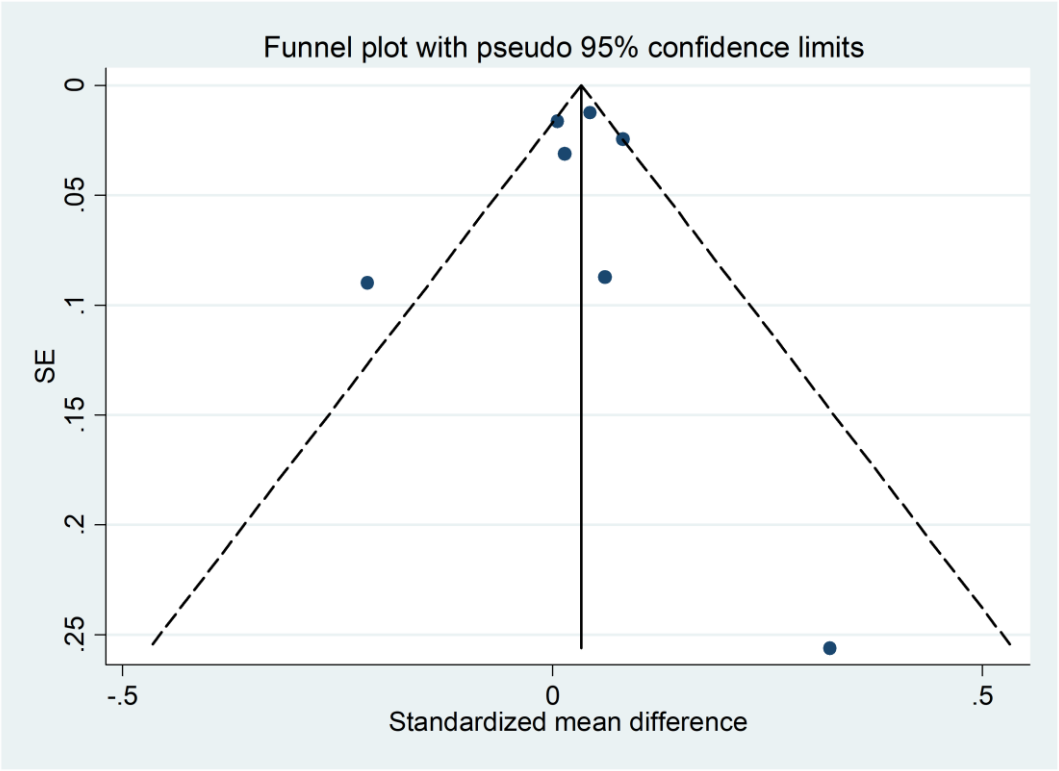
Supplementary Figure 2A: Meta-analysis of studies examining the relationship between the legalisation of cannabis for medical purposes and levels of use in adolescents and young adults (12-25 years, prior to March 2018).



Supplementary Figure 2B: Funnel plot of studies examining the relationship between legalisation of cannabis for medical purposes and levels of use in adolescents and young adults (12-25 years, I^2=98.6%, prior to March 2018).



Supplementary Figure 3A: Meta-analysis of studies examining the relationship between the legalisation of cannabis for recreational purposes and levels of use in adolescents and young adults (12-25 years, prior to March 2018).



Supplementary Figure 3B: Funnel plot of studies examining the relationship between legalisation of cannabis for recreational purposes and levels of use in adolescents and young adults (12-25 years, I^2=45.0%, prior to March 2018).

PRISMA-DTA Checklist

Section/topic	#	PRISMA-DTA Checklist Item	Reported on page #
TITLE / ABSTRACT			
Title	1	Identify the report as a systematic review (+/- meta-analysis) of diagnostic test accuracy (DTA) studies.	1 & 2
Abstract	2	Abstract: See PRISMA-DTA for abstracts.	2-3
INTRODUCTION			
Rationale	3	Describe the rationale for the review in the context of what is already known.	5-6
Clinical role of index test	D1	State the scientific and clinical background, including the intended use and clinical role of the index test, and if applicable, the rationale for minimally acceptable test accuracy (or minimum difference in accuracy for comparative design).	6
Objectives	4	Provide an explicit statement of question(s) being addressed in terms of participants, index test(s), and target condition(s).	6
METHODS			
Protocol and registration	5	Indicate if a review protocol exists, if and where it can be accessed (e.g., Web address), and, if available, provide registration information including registration number.	6-8
Eligibility criteria	6	Specify study characteristics (participants, setting, index test(s), reference standard(s), target condition(s), and study design) and report characteristics (e.g., years considered, language, publication status) used as criteria for eligibility, giving rationale.	7-8
Information sources	7	Describe all information sources (e.g., databases with dates of coverage, contact with study authors to identify additional studies) in the search and date last searched.	6-7
Search	8	Present full search strategies for all electronic databases and other sources searched, including any limits used, such that they could be repeated.	6-7
Study selection	9	State the process for selecting studies (i.e., screening, eligibility, included in systematic review, and, if applicable, included in the meta-analysis).	6-7
Data collection process	10	Describe method of data extraction from reports (e.g., piloted forms, independently, in duplicate) and any processes for obtaining and confirming data from investigators.	8
Definitions for data extraction	11	Provide definitions used in data extraction and classifications of target condition(s), index test(s), reference standard(s) and other characteristics (e.g. study design, clinical setting).	8
Risk of bias and applicability	12	Describe methods used for assessing risk of bias in individual studies and concerns regarding the applicability to the review question.	6-7
Diagnostic accuracy measures	13	State the principal diagnostic accuracy measure(s) reported (e.g. sensitivity, specificity) and state the unit of assessment (e.g. per-patient, per-lesion).	N/A
Synthesis of results	14	Describe methods of handling data, combining results of studies and describing variability between studies. This could include, but is not limited to: a) handling of multiple definitions of target condition. b) handling of multiple thresholds of test positivity, c) handling multiple index test readers, d) handling of indeterminate test results, e) grouping and comparing tests, f) handling of different reference standards	8-9

PRISMA-DTA Checklist

Section/topic	#	PRISMA-DTA Checklist Item	Reported on page #
Meta-analysis	D2	Report the statistical methods used for meta-analyses, if performed.	8-9
Additional analyses	16	Describe methods of additional analyses (e.g., sensitivity or subgroup analyses, meta-regression), if done, indicating which were pre-specified.	8-9
RESULTS			
Study selection	17	Provide numbers of studies screened, assessed for eligibility, included in the review (and included in meta-analysis, if applicable) with reasons for exclusions at each stage, ideally with a flow diagram.	9-10
Study characteristics	18	For each included study provide citations and present key characteristics including: a) participant characteristics (presentation, prior testing), b) clinical setting, c) study design, d) target condition definition, e) index test, f) reference standard, g) sample size, h) funding sources	10-11, Tables 1, 2&3
Risk of bias and applicability	19	Present evaluation of risk of bias and concerns regarding applicability for each study.	11-14
Results of individual studies	20	For each analysis in each study (e.g. unique combination of index test, reference standard, and positivity threshold) report 2x2 data (TP, FP, FN, TN) with estimates of diagnostic accuracy and confidence intervals, ideally with a forest or receiver operator characteristic (ROC) plot.	N/A
Synthesis of results	21	Describe test accuracy, including variability; if meta-analysis was done, include results and confidence intervals.	11-12; 13; 14
Additional analysis	23	Give results of additional analyses, if done (e.g., sensitivity or subgroup analyses, meta-regression; analysis of index test: failure rates, proportion of inconclusive results, adverse events).	11-12; 13; 14
DISCUSSION			
Summary of evidence	24	Summarize the main findings including the strength of evidence.	14-15
Limitations	25	Discuss limitations from included studies (e.g. risk of bias and concerns regarding applicability) and from the review process (e.g. incomplete retrieval of identified research).	15-17
Conclusions	26	Provide a general interpretation of the results in the context of other evidence. Discuss implications for future research and clinical practice (e.g. the intended use and clinical role of the index test).	18-19
FUNDING			
Funding	27	For the systematic review, describe the sources of funding and other support and the role of the funders.	N/A

Adapted From: McInnes MDF, Moher D, Thombs BD, McGrath TA, Bossuyt PM, The PRISMA-DTA Group (2018). Preferred Reporting Items for a Systematic Review and Meta-analysis of Diagnostic Test Accuracy Studies: The PRISMA-DTA Statement. JAMA. 2018 Jan 23;319(4):388-396. doi: 10.1001/jama.2017.19163.

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